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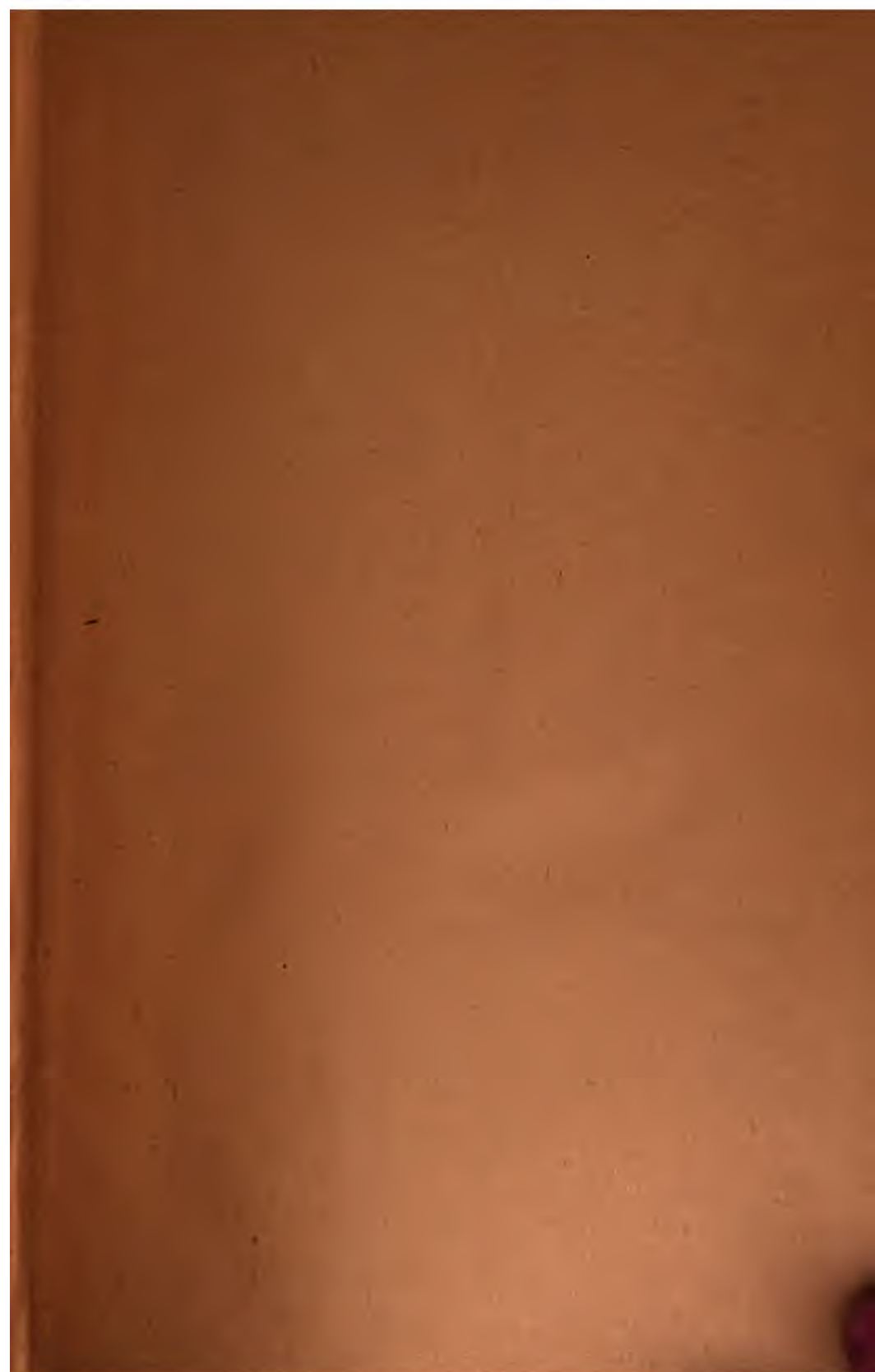
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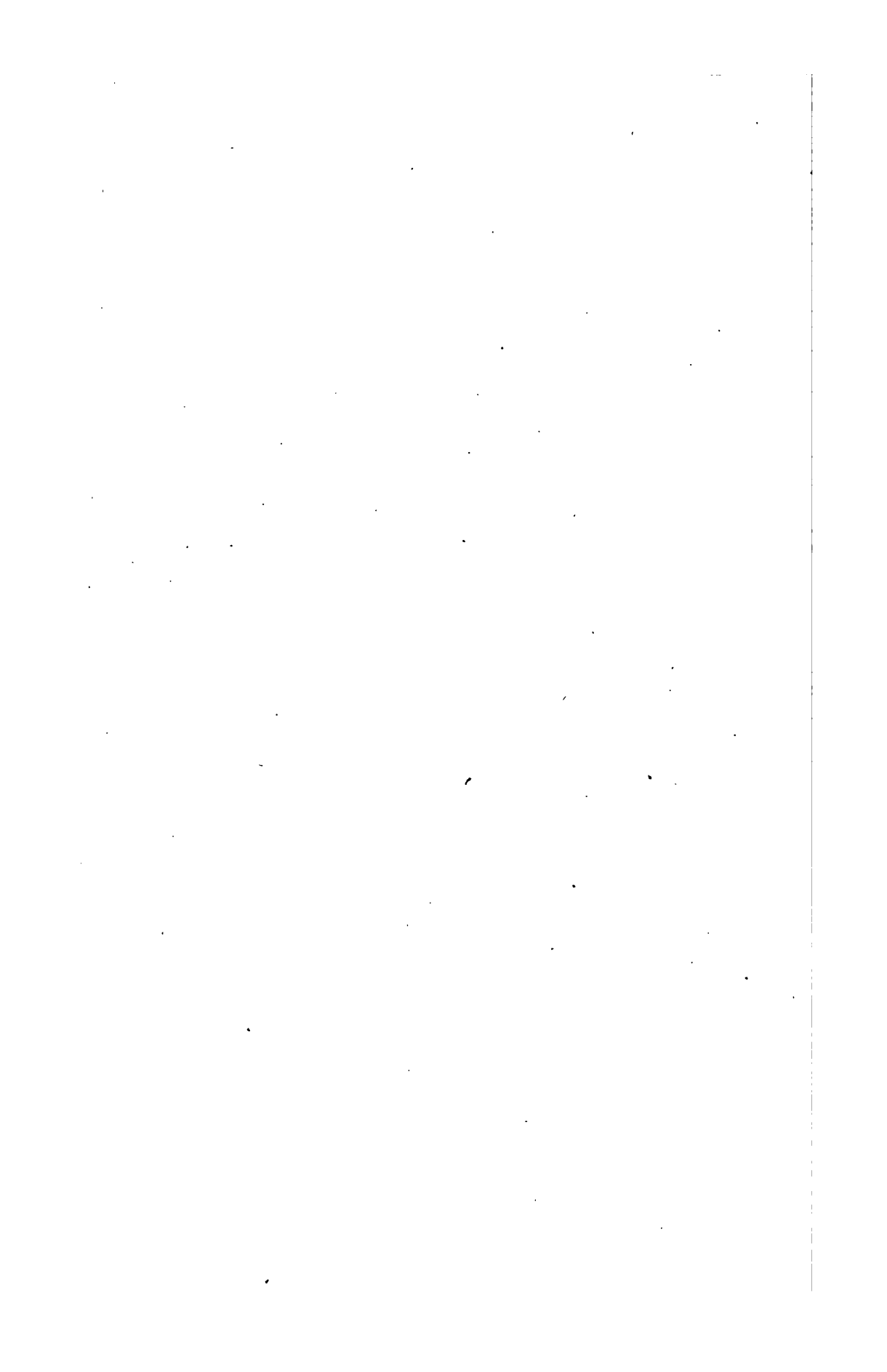
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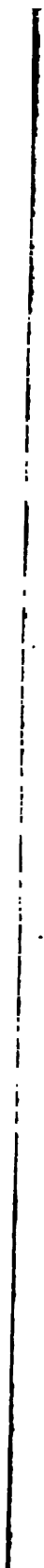


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YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN,
SURGEON-GENERAL M. H. S.,
Chairman.

H. D. GEDDINGS,
PASSED ASSISTANT SURGEON, M. H. S.,
Secretary.

BULLETIN No. 1.

REPORT ON ORGANIZATION AND PROGRESS OF THE INSTITUTE.

(ABSTRACT OF MINUTES.)

MARCH, 1902.

YELLOW-FEVER INSTITUTE OF THE U. S. MARINE-HOSPITAL SERVICE.

In view of the importance of the definite determination of the cause, means of spread, history and statistics, and quarantine management and therapeutic treatment of yellow fever, it was determined to form within the U. S. Marine-Hospital Service an Institute for the investigation of these problems and other kindred topics which might be found to have a bearing on the questions as investigations proceeded.

The prime object of the organization is to stimulate the spirit of scientific investigation among officers of the corps and to secure the cooperation of all who are interested in the solution of these very important questions.

On September 13, 1901, a plan of organization was submitted to the honorable Secretary of the Treasury, which, receiving his approval, led to the organization of the Institute, with an executive board, constituted as follows :

CHAIRMAN OF THE INSTITUTE.

The SURGEON-GENERAL OF THE U. S. MARINE-HOSPITAL SERVICE.

SECRETARY.

Passed Asst. Surg. H. D. GEDDINGS, M. H. S., in Charge of the Bureau Division of Scientific Research.

CHAIRMEN OF SECTIONS.

SECTION A—*History and Statistics*.—Chairman, Surg. George T. Vaughan, M. H. S., In Charge of Bureau Division of Sanitary Reports and Statistics.

SECTION B—*Etiology*.—Chairman, Passed Asst. Surg. M. J. Rosenau, M. H. S., Director of the Hygienic Laboratory, M. H. S.

SECTION C—*Transmission*.—Chairman, Surg. J. H. White, M. H. S., In Charge of Bureau Division of Domestic Quarantine.

YU. A. IZRAEL

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December 3, 1901.—At a meeting of the Executive Board letters were read from Asst. Surg. R. H. von Ezdorf and Passed Asst. Surg. G. M. Guitéras, nominating certain gentlemen as members of the Institute. Upon motion they were elected as members, and the secretary was instructed to so notify them.

A report was received from Acting Asst. Surg. Owen W. Stone, relative to an epidemic of yellow fever at Greenville, Miss., in 1878, supposed to have originated from infected baggage from New Orleans.

The chairman of Section B offered to the Institute for use as a bulletin a report by Assistant Surgeon Grubbs on "Mosquitoes in Baggage," which the secretary was ordered to prepare for publication.

January 21, 1902.—A proposition was received from Drs. O. L. Pothier and George E. Beyer, of New Orleans, La., offering to place themselves at the disposal of the Institute and the Service, with a view of continuing the work which they had already done, as members of the Orleans Parish Mosquito Commission, said work to be in the interest and on behalf of the Institute of which they are members.

Discussion followed, in which it was agreed that it would be advantageous to engage the services of these gentlemen, and to associate with them Asst. Surg. H. B. Parker, M. H. S., the three to constitute a working party, who would proceed to some point in Mexico or South America, when and where yellow fever might make its appearance, for the purpose of continuing the work inaugurated by the New Orleans commission. It was directed that Drs. Pothier and Beyer be communicated with, and a definite proposition obtained from them.

It was further agreed that it would be advisable to station an officer for purposes of observation in Habana, Cuba, and the Surgeon-General M. H. S., was requested, if possible, to detail Asst. Surg. D. H. Currie for the purpose, he having received special training which would fit him for the detail.

Attention was also called to the presence of the French commission for the investigation of the cause of yellow fever, which was at present located at Petropolis, in Brazil.

It was further agreed that it would be advisable to keep informed as to the prevalence of yellow fever on the west coast of Africa (Senegal), with a view to dispatching another worker or party to that point.

Information was also elicited to the effect that the services of Acting Assistant Surgeon Gregory, who is now undergoing instruction in the Hygienic Laboratory, and whom it was intended to dispatch to Rio de Janeiro, would be of value in enabling him to report upon such transactions of the French commission as might come to his notice.

A report was read from the consul at Marseille, France, showing the quarantine management of yellow fever at that port, and giving statistics of the disease for past years.

January 29, 1902.—At a meeting of the executive board, the secretary read a communication received from Drs. Pothier and Beyer of New Orleans, in which they expressed a perfect willingness to have Dr.

Parker associated with them, and in which they also proposed terms, etc. These terms and proposed arrangements being considered reasonable and advantageous, it was resolved that the Surgeon-General Marine-Hospital Service be requested to have Drs. Pothier and Beyer appointed temporary acting assistant surgeons for the purpose, and on the terms named by them. The question of the publication of bulletins was again brought before the meeting, and it was decided informally that an effort should be made to prepare a general bulletin showing the progress of organization, and that this should be succeeded by special bulletins, showing the work of the various sections, material for some of these special bulletins being now in the hands of the secretary and further additions being promised.

February 14, 1902.—At a meeting held this day the names of Dr. Pedro J. Salierup and Dr. Antonio Molina, of Ponce, P. R., were submitted for membership by letter from Asst. Surg. W. W. King and upon motion duly seconded they were elected to membership. Upon motion duly seconded, Dr. George H. F. Nuttall, of Cambridge, England, was invited to membership in the Institute, and the secretary was instructed to convey notice of the invitation to him by letter.

Upon motion made and duly seconded, the following foreign scientists were invited to enroll themselves as corresponding members of the Institute: Drs. N. del Rio, Manuel Iglesias, and Z. Molina, of Vera Cruz, Mexico; Prof. Guiseppe Sanarelli, of the University of Bologna, Italy; Dr. Catalan, chief of quarantine, of Marseille, France; Professor Proust, Inspector General of the Sanitary Service of the Republic of France; Professor Wurtz, of the School of Medicine, Paris, France; Dr. E. Liceaga, President of the Superior Board of Health of Mexico; Dr. Frederick Montizambert, Director General of Public Health, Ottawa, Ontario; Dr. W. Havelburg, of Berlin, Germany; Prof. R. Blanchard, of the Faculty of Medicine, Paris, France, and Professor Dunbar, of the Hygienic Institute, Hamburg, Germany.

Dr. Vaughan then reported that he had received from Assistant Surgeon Glover, at Boston, Mass., a contribution on the question "Why Did Not New Orleans have Yellow Fever in Early Times, while Boston Did," and suggested its publication as a special bulletin from Section A, which was so ordered. He further reported that he was in receipt of two papers from Passed Asst. Surg. J. M. Eager, at Naples, Italy, one being a general history of yellow fever in Europe, the other a history of the disease in Portugal, with a promise of further contributions on the subject of the disease in other countries in Europe. He suggested, and it was ordered, that these be published also as special bulletins.

Surgeon White reported that as chairman of Section C he was in receipt of a contribution from Surg. H. R. Carter on the subject of the infection of ships by yellow fever—the result of personal observations. After considerable discussion it was agreed that the article should be offered to a medical journal for publication, and that it should subsequently appear as a special bulletin of the Institute.

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Attention was also called to the presence of the French commission for the investigation of the cause of yellow fever, which was at present located at Petropolis, in Brazil.

It was further agreed that it would be advisable to keep informed as to the prevalence of yellow fever on the west coast of Africa (Senegal), with a view to dispatching another worker or party to that point.

Information was also elicited to the effect that the services of Acting Assistant Surgeon Gregory, who is now undergoing instruction in the Hygienic Laboratory, and whom it was intended to dispatch to Rio de Janeiro, would be of value in enabling him to report upon such transactions of the French commission as might come to his notice.

A report was read from the consul at Marseille, France, showing the quarantine management of yellow fever at that port, and giving statistics of the disease for past years.

January 22, 1902.—At a meeting of the executive board, the secretary read a communication received from Drs. Pothier and Beyer of New Orleans, in which they expressed a perfect willingness to have Dr.

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Surgeon White reported that as chairman of Section C he was in receipt of a contribution from Surg. H. R. Carter on the subject of the infection of ships by yellow fever—the result of personal observations. After considerable discussion it was agreed that the article should be offered to a medical journal for publication, and that it should subsequently appear as a special bulletin of the Institute.

The chairman of Section D reported that a letter had been addressed through the Treasury Department to the Department of State, requesting that the consuls in various Central and South American districts be requested to give early telegraphic notice of the appearance of yellow fever in their localities, in order that the Institute might make proper arrangements to dispatch its working parties to the scene of the outbreak.

February 26, 1902.—The secretary reported that in the matter of the invitations to foreign scientists to enroll themselves as corresponding members, it had been deemed expedient by the Surgeon-General to request the Secretary of the Treasury to ask the opinion of the Department of State as to the propriety of issuing invitations to such gentlemen, several of whom were actually officials under their various governments. The matter was therefore held in abeyance, pending the receipt of this decision, but a reply having been received from the Secretary of State, stating that the proposed action was in accord with official propriety, the invitations were subsequently duly dispatched.

The secretary further reported that a reply had been received from the Department of State, saying that in accordance with request, the consuls at Rio de Janeiro, Santos, and Vera Cruz had been instructed to cable information of the first appearance of yellow fever in their districts.

The Surgeon-General was requested to take the necessary preliminary steps toward having Drs. Beyer and Pothier, of New Orleans, nominated in due form as acting assistant surgeons, in order that there might be no delay in dispatching them when an outbreak of yellow fever made the employment of their services desirable.

A discussion followed on the most recent announcement by Drs. Reid and Carroll of their work on the etiology of yellow fever, who announced as a result of their experiments, that the causative organism of yellow fever was ultra-microscopical.

While all officers of the Marine-Hospital Service are *de facto* members, at this time the Institute has as members 55 officers of the Marine-Hospital Service, who have formally given notice of their cooperation. Assurances of cooperation have been received from the Surgeons-General of the United States Army and Navy, and in addition to those invited and enrolled as corresponding members, over 100 invitations to membership have been issued and acknowledged, including bacteriologists and pathologists, secretaries and executive officers of State and local boards of health, the president and secretary of the American Medical Association, and the chairman and secretary of the section of hygiene and sanitary science of the same association, members of the committee on the etiology of yellow fever of the American Public Health Association, and physicians in all parts of the United States, Cuba, and Porto Rico.

The names of all those elected to membership are not included in the foregoing transcript, but in a subsequent bulletin there will appear a full list of the regular and corresponding members of the Institute.

YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN No. 2.

Section A.—HISTORY AND STATISTICS.

Surg. GEORGE T. VAUGHAN, Chairman of Section.

YELLOW FEVER—WHY DID NOT NEW ORLEANS HAVE INVASIONS OF THE DISEASE IN EARLY TIMES, WHILE BOSTON DID?

By M. W. GLOVER, *Assistant Surgeon, M. H. S.*

MARCH, 1902.

YELLOW FEVER—WHY DID NOT NEW ORLEANS HAVE IT IN EARLY TIMES, WHILE BOSTON DID?

In the consideration of this subject it is necessary, first to ascertain the date of the primary visitation of yellow fever in the two cities. After a careful examination of the authorities, one arrives at the conclusion that the first undoubted visit of yellow fever to Boston was in 1798. In 1693 the following circumstances, quoted from Hutchinson, have given rise to the statement that yellow fever prevailed in that year in Boston. An English fleet had been ordered from the West Indies to Boston to cooperate with land forces in an attack on Quebec.

Before Sir Francis Wheeler came to Boston with the fleet, June 17, 1693, he had buried 1,300 out of 2,100 sailors, and 1,800 out of 2,400 soldiers. * * * The distemper, which had been in the fleet spread to Boston, and was more malignant even than the smallpox had been or any other epidemical sickness which had been in the country before.

Chief Justice Sewall, in his diary, also remarks on the deaths of several persons from the "sickness of the fleet."

On the other hand Cotton Mather in his *Magnalia*, says:

There was an English fleet of our good friends, with a direful plague aboard, intended hither. Had they come, as they intended, what a horrible desolation had cut us off, let the desolate places that some of you have seen in the colonies of the South declare unto us! And that they did not come, was the signal hand of Heaven.

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Noah Webster, in his *History of Pestilential and Epidemic Diseases* (1799), arrives at the following conclusion :

From this authentic history, written by a contemporary clergyman, we infer that Hutchinson must have made a mistake. Sir Francis Wheeler's fleet arrived at Boston most dreadfully infected, but no disease was propagated in Boston. Some other fleet, it seems, had introduced the disease into "a colony of the South," perhaps Newport or New York, but I have no information on the subject.

Lyman Spalding, in *Reflections on Yellow Fever Periods* (1819), states that the first appearance of yellow fever in Boston was on the 25th of August, 1796, "in a family at the southeasterly part of the town, near a considerable extent of flats, which are daily exposed for some hours to the action of the sun. No mention is made of importation either by Dr. Warren or by Dr. Brown. Public opinion did not even accuse any vessel of having imported it." Noah Webster says that in 1796 the disease appeared in Boston, but was not general or severe. "It spread only in a small part of the town adjoining the water." This occurrence, if of true yellow fever, was undoubtedly sporadic.

This brings us, then, to the first undoubted epidemic of yellow fever in Boston, which occurred in 1798. With regard to the origin of this epidemic, the following statement is made in Tytler's *Treatise on Plague and Yellow Fever* (1799).

The origin of the fever at Boston has, as usual, been disputed, but the common opinion is that it was generated. It now appears, however, that, though there are very strong reasons for supposing it to have originated in the place, there are others equally strong for believing that it was imported. It is ascertained that a vessel, on board which persons had died with the yellow fever, lay in the neighborhood of the family first seized with the disease in 1798.

Dr. Warren dismisses the subject thus: "No person could produce any evidence of importation of this disease." Noah Webster says that the fever showed most violent effects in the region of Fort Hill, and suggests that we may find the cause in the very extensive flat between Boston and Dorchester Point, which is uncovered at low water. In common with all the other cities afflicted by epidemics from 1793 to 1804, yellow fever in Boston began in the most filthy part of the town. Mill Pond, one of the foci of the disease, is thus described by Samuel Brown :

This pond is the common receptacle of a great number of dead dogs, cats, and small animals, besides large quantities of putrid meat, fish, and vegetables. There also empty the sewers and drains from vaults and cellars of the buildings surrounding the place. This pond was frequently, during the summer, deprived of its waters, and its naked surface exposed to the excessive heat of the sun.

Fever prevailed until the latter part of October, when a severe northeaster, continuing for three days, followed later by a heavy frost, completely checked the disease.

That our forefathers in medicine were puzzled by the eccentricities of this disease there is abundant proof in the literary remnants of a bitter controversy as to whether yellow fever was imported or domestic,

whether it was contagious or noncontagious. One thing is to be borne in mind in considering the sporadic cases of the years previous to 1798, and that is the possibility of a mistaken diagnosis. We have positive proof that malarial fevers were common in New England in the early days, though now malaria is no longer endemic in this region, possibly due to the filling in of stagnant ponds and improved drainage facilities. In view of all the circumstances we are justified in considering 1798 as the earliest appearance of yellow fever in Boston.

Let us now consider New Orleans. This city was founded by Bien-ville in 1718, though it was not until 1722 that the capital was finally established there. It was not for many years after the settlement of Louisiana that the attention of its people was given to the development of its agricultural resources, and commerce with other countries entered into. Yellow fever seems to have been unknown in New Orleans until 1769, when an outbreak occurred, which was not general and appears to have been sporadic. In one place a statement is made that yellow fever was introduced in this year by a British vessel from the coast of Africa with a cargo of slaves. No confirmation of this statement could be found, however. In 1796, according to Chaillé, occurred the first epidemic of yellow fever, and he considered the digging of the Carondelet Canal, begun in 1794, as a predisposing factor. In a work entitled, *Travels in Louisiana and the Floridas*, published in 1802, it is stated that yellow fever was unknown in New Orleans prior to 1796, and "it is the general opinion that the yellow fever at New Orleans was imported from the United States of America. * * * It is thought to have its origin from the fever that committed its ravages at Philadelphia in 1793, and that it was brought to New Orleans by the Americans themselves," who engaged the greater part of the trade of New Orleans.

From the foregoing it will be seen that, disregarding all sporadic cases, Boston had its first epidemic in 1798, New Orleans in 1796. Therefore, there was little, if any, difference in the time of the advent of yellow fever in both cities. It seems that both were touched by the great wave of pestilence that swept over the country from 1793 to 1804. In Boston the disease was as seed that fell in stony places and, having no root, withered away; while in New Orleans it was as seed that fell on good ground and brought forth fruit an hundredfold, bearing its yearly crop of deaths and desolation.

If we consider sporadic cases, however, the conclusions we arrive at are not materially different. In 1691 and 1693, when Boston is reputed to have had yellow fever, New Orleans did not have it for only one reason, and that was the nonexistence of New Orleans. From 1718, the date of New Orleans' birth, until 1796, the first epidemic in the city, Boston was equally free from the visits of the pestilence.

YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 3.

Section A.—HISTORY AND STATISTICS,

Surg. GEORGE T. VAUGHAN, Chairman of Section.

YELLOW FEVER IN EUROPE—A GENERAL HISTORICAL REVIEW.

By J. M. EAGER. *Passed Assistant Surgeon, M. H. S.*

MARCH, 1902.

YELLOW FEVER IN EUROPE.

Although the fact is well known that at various times yellow fever has gained a foothold in Europe, no adequate idea can be had of its widespread prevalence at many places where it has been introduced except by a careful review of the literature of the disease. The extent of some of these accidental epidemics of yellow fever occurring outside of the regions of its periodic prevalence is made evident when it is remembered that at Barcelona, Spain, during the funereal epidemic of the year 1821, approximately 25,000 persons died within five months of yellow fever, and that, at Lisbon, Portugal, during the year 1857, in an epidemic of five months' duration, there were over 13,000 persons stricken with the disease, the mortality being almost 50 per cent.

An outbreak of bubonic plague in a European city as disastrous as, for example, the yellow fever epidemics mentioned would certainly give, rise to the justifiable apprehension that the disease was likely to overrun the Continent.

That the mosquito conveys the yellow fever infection, according to the theory of Finlay, appears to be satisfactorily proved. In event of the fact being further established that the mosquito is the sole agent in the transmission of the infection of yellow fever from man to man, it would be interesting to know what particular mosquito was instrumental in the spread of the disease after its introduction into European ports. From the review of the literature of the subject, and such inquiries as have been made in the preparation of this writing, it has

spread throughout the shipping of the port, infecting 7 other vessels, with a result that 40 persons fell ill of yellow fever and 23 died, has led a recent writer (de Gouvea, *Le Bulletin Medical*, October 12, 1901) to observe that the facts, in his opinion, adapt themselves perfectly to the theory of the propagation of yellow fever by mosquitoes. On different occasions, after the epidemic at Saint Nazaire, yellow fever occurred on board ships in French harbors, but did not appear ashore, except in 1870, when a seaman from a pest ship died of yellow fever in a civil hospital at Marseille.

The yellow fever history of the British Isles is limited to 5 appearances of the disease between the years of 1817 and 1865, in the harbors of Falmouth, Southampton, and Swansea.

At Leghorn, in 1804, yellow fever was introduced by a Spanish vessel from Alicante and Cadiz where the disease was epidemic. The disease prevailed at Leghorn for four months, causing not less than 700 deaths, and according to one author as many as 1900. At Torre Annunziata, a city of 20,000 inhabitants situated in the province of Naples, there was in 1883 an epidemic prevalence of a disease which was pronounced by several competent medical men to have been yellow fever. Of 13 cases presenting clinical features at least closely resembling yellow fever, 7 died. A full epidemiological account of the disease, gathered from the municipal archives of Torre Annunziata, has been prepared for the present writing. This interesting epidemic outbreak was completely lost sight of, and for the time apparently forgotten in the overshadowing gloom of the terrible cholera epidemic 1884, at Naples, on the eve of which it occurred.

The history of yellow fever in Europe closes in 1894, with the death from that disease of two seamen in a hospital at Trieste. The contagion was brought to Austria from Brazil by two sailors who landed from a pest ship at Genoa and went by land to Trieste.

In the examination of literature for the preparation of this account, it was found that the epidemiology of yellow fever is not anywhere collected in a single writing. It is scattered through many books. A comprehensive survey of the subject is of more than antiquarian interest. It has at least the value of teaching that the disease is capable of extending, under suitable conditions, and prevailing epidemically in Europe, as it did in Philadelphia and other Northern cities of the United States, a century ago.

With a view to presenting in a summary manner the epidemiology of yellow fever in Europe, this account has been prepared from the extensive and scattered literature of the subject.

YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN No. 4.

Section A—HISTORY AND STATISTICS

Surg. GEORGE T. VAUGHAN, Chairman of Section.

YELLOW FEVER IN PORTUGAL.

By J. M. EAGER, *Passed Assistant Surgeon, M. H. S.*

MARCH, 1902.

YELLOW FEVER IN PORTUGAL.

1723. In the year 1723, yellow fever was imported into Lisbon from Brazil and, according to documents in possession of the sanitary council of the Kingdom of Portugal, this was the first appearance of yellow fever in Europe. At that time Lisbon had a population much smaller than at the period of the great epidemic of 1857. Still the number of persons said to have been taken ill with the disease and the mortality during the first epidemic were greater than in the latter. There is, however, no accessible document giving specific information on the subject.

1850. At Oporto, in July, 1850, the ship *Edward IV* arrived from Brazilian ports infected with yellow fever. Some of the custom-house officers, sent on board in the discharge of their duties, were attacked with the disease, and of 5 stricken, 3 died. The sanitary authorities, with a view to averting a panic, tried to prevent the truth being known, and for a time succeeded in concealing the facts. Fortunately the malady did not spread widely. The disease was confined to the localities in which the custom-house employees lived.

1851. In the year 1851, there arrived at Oporto, the ship *Tentadora*, coming from Rio de Janiero. During the voyage, 5 of the crew had been attacked with yellow fever. Several of the custom-house employees who went aboard the ship at Oporto were taken sick and died of yellow fever. The ship *Edward IV*, which during the previous year had

brought yellow fever to Oporto, again arrived at that port, September 10, having had deaths aboard from yellow fever during the voyage. The vessel spent twelve days in quarantine. After being given pratique, 2 custom-house men posted aboard to guard the ship were attacked with the disease and promptly died. A little later, 3 laborers employed in removing the cargo from the hold, and several other persons who had been on the vessel, were taken ill with the same malady. The disease afterwards spread in the quarters known as Miragaia and Massarellos and altogether 17 persons died in consequence. At this point, there arrived from Brazil another vessel, the *Santa Cruz*. The same malady was repeated among the custom-house employees, the stevedores, and other persons who in one way or another had had direct relation with the infected ship. The popular alarm occasioned by these frequent appearances of fatal cases resulted in the appointment of a sanitary commission for the study of the matter and the recommendation of measures of betterment. Notwithstanding the vigorous means adopted to this end, cases continued to occur. The infection spread to 2 British vessels anchored down the wind from the pest ship *Santa Cruz*. The British vessels were supposed to be quite isolated from the *Santa Cruz*. Soon other cases appeared on 2 Portuguese vessels anchored to leeward of the British vessels. Several of the men of the Portuguese vessels died. The epidemic lasted a short time only, but there were 40 deaths.

1856. The third epidemic occurred in 1856. Early in July some vessels arrived from Brazil, where yellow fever prevailed. July 12 the first cases appeared, and, as before, the first persons affected were custom-house employees, stevedores, and those in contact with the suspicious vessels. Again a focus of infection was established in the Miragaia quarter. There were also cases of yellow fever among the soldiers of the municipal garrison, but a marked difference was noted, both in the intensity of the symptoms and in the issue of the disease between the cases falling ill on board ship and those resulting from contact with infected persons and things. The first cases were congregated in a special hospital, and of these, 16 out of 21 died. On the other hand, only 10 deaths took place among the 27 soldiers attacked. Energetic measures were taken by the authorities of the port. The pest-ridden vessels were isolated and carefully disinfected. Certain of the vessels, being evidently deemed infected beyond hope of cleansing, were sunk at sea. This epidemic began July 21 and ended October 2, 1856. A total of 120 cases and 63 deaths resulted from the outbreak.

Belem is a small town not far from Lisbon. It was the seat of the lazaretto during the epidemic at Oporto. An extension of the epidemic began by the death from yellow fever of the wife of a pharmacist at Belem. This case was followed by others at considerable intervals, and finally an epidemic established itself. The disease was mistaken for typhus fever by the local physicians, but the members of the royal

commission that investigated the pestilence found that at least some of the cases presented the undoubted characteristics of yellow fever. There was an epidemic of Asiatic cholera at Lisbon in 1855, and the disease had not entirely disappeared in 1856, though it had diminished and was already decreasing. At about the time of the disappearance of the cholera, some cases of fever appeared in Lisbon having the same symptoms and epidemic characteristics of the yellow fever at Belem.

1857. In the year 1857, Lisbon had a population of 200,000 inhabitants. Preceding the period of the yellow-fever outbreak of 1857 the public health had been excellent. The mortality rate was less than for the corresponding period of the previous year. A commission delegated to make a report of the epidemic could not determine to a certainty whether the disease was imported by sea or came from the infection of former epidemics in Portugal. In March, the steamship *Tamar* had lost 2 men from yellow fever on a voyage from Brazil to Portugal. The steamship only touched at Portuguese ports, leaving immediately for England. It appears that it was this steamer that carried yellow fever to Southampton, a circumstance that will be referred to under another head. The vessel returned to Lisbon in the month of September. Early in July, a steamer called the *Genora* arrived at Lisbon, bringing immigrants from Brazil. Many of these persons were so ill that all of them were sent at once to Belem to pass the period of quarantine in a lazaretto. In the beginning of July, a seaman from the *Algarve* fell ill in the house where he lodged, and shortly after 9 persons sickened of the same disease in the same house. The commission reported that it was impossible to state what was the outcome of the disease in these 10 cases, from which it may be inferred that they were spirited away in the interest of their neighbors. At Lisbon, immigrant baggage and effects were stored in dirty and badly ventilated places. They contained trunks with the miscellaneous effects and soiled clothes of immigrants, packages of rags, and sundry articles, many of them evidently filthy from human vomit, sputum, and feces. July 22, a person employed at the baggage division of the customs service was taken ill and died in five days with the symptoms of yellow fever. July 29, a woman who had been in frequent contact with the customs employees fell sick and was dead in five days. From this moment, cases began to multiply in the localities where the first cases were treated. Neighboring habitations were in turn invaded, and finally whole streets and quarters of the town became filled with cases. Ultimately, distant foci developed, originating evidently from persons in contact with yellow-fever patients.

While in the city the epidemic was assuming gigantic proportions, the health of the harbor remained perfectly good. No suspicious cases were reported on board of vessels anchored in the harbor, nor among the public servants stationed on or near the water, to guard the port and shipping. From these facts, the royal commission concluded that

the infection had been introduced, not by the vessels or their personnel, but by filthy fomites deposited in the customs magazines of the ports.

During this epidemic, 13,757 persons were ill with the disease, and 5,652 died. Of the 5,915 cases treated in hospital, 1,932 died. Of the 7,482 treated at their homes, 3,466 died. The other deaths evidently occurred among vagabonds and those who succumbed in public places not under medical control. The relative proportion of the cases to the inhabitants was 1 to 35.4; the proportion of cases of yellow fever to other diseases was 1 to 3.18. Of the 3,466 who died at their homes, 2,061 were males and 1,405 females. The mortality was much greater in proportion to the number affected among adults than among children. Most of the old persons who were stricken died. The commission noted that occupation had no influence in imparting the disease except in so far as it involved exposure in the open air during the night. The fastigium of the epidemic was reached during the month of October. At the beginning of the epidemic, the disease in individual cases ran its course in from fifteen hours to five days. Later in the epidemic the disease lasted longer in the fatal cases as well as in those that ended in recovery. In the hospitals, the greater number died during the first three days of the disease, and as the disease progressed there was a constantly diminishing mortality. The accessible hospital records give the following showing:

Discharged three days after admission.....	344
Discharged five days after admission.....	357
Discharged seven days after admission.....	762
Discharged eleven days after admission.....	788
Discharged fifteen days after admission.....	345

A few only remained in the hospital for a month or more. Of persons employed about the hospitals, one-sixth were taken sick with the disease and among these there was a mortality of 25 per cent. It was especially remarked that at the gas works, where illuminating gas was produced, not a single case of yellow fever occurred among the employees, although the trade exposed the workers to the night air. In this connection it is interesting to consider whether it might not be that illuminating gas or other products evolved in its manufacture served to kill mosquitoes, spoil their appetite for human blood, or at least keep them at a distance.

During the epidemic at Lisbon there were 112 cases of yellow fever in the neighboring city of Olivæ, which at the time had 23,000 inhabitants. Sixty of the sick persons were fugitives from Lisbon. In other neighboring places scattered cases developed. It was remarked that the quality and direction of the wind had no perceptible influence in the propagation of the disease. The epidemic commenced July 22 and was declared finished December 10, 1857.

1858. During the months of January, February, and March, 1858, cases of yellow fever were reported at intervals in Lisbon. In consequence, a total of 11 deaths were attributed to the disease.

1858. At Vigo, Fereol, Oporto, and at Ponta Delgada, in the Azores, cases of yellow fever were imported by vessels arriving from Brazil, in 1858. The sick persons were promptly isolated and the disease did not spread.

YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN NO. 5.

Section A.—HISTORY AND STATISTICS.

Surgeon, GEORGE T. VAUGHAN, Chairman of Section.

YELLOW FEVER IN SPAIN.

By J. M. EAGER, *Passed Assistant Surgeon, M. H. S.*

MARCH, 1902.

YELLOW FEVER IN SPAIN.

In connection with the first appearance of yellow fever in Spain, the interesting question arises of the initial occurrence of yellow fever in Europe. According to Moreau de Jonnes, the primary importation into Spain was in 1705. If this were true, Spain could claim to be the first European country afflicted with the disease, for the story of the alleged outbreak at La Rochelle, France, in 1700, lacks scientific authority. Villalba, the famous Spanish epidemiologist, maintains, however, that the original introduction into Spain took place in 1730. In this opinion all the writers of importance who have succeeded Villalba thoroughly concur. So that, in the light of all available evidence, it must be considered that the initial advent of yellow fever in Europe was at Lisbon, Portugal, in 1723.

1730. In the year 1730 a ship from the Americas brought to Cadiz a malady never before seen in that city. The disease was characterized by a malignant fever, a yellow discoloration of the skin, and, in the last stages of fatal cases, by black vomit. Many persons were stricken with the malady, and the epidemic diffused itself through other cities of Spain.

1733. At Cadiz the disease was again imported in 1733, but the prevalence was not extensive.

1741. A vessel from the Antilles landed a large cargo of merchandise at Malaga. Immediately afterwards a pestilential malady was evolved,

a disease exhibiting the same aspects as the fever at Cadiz in 1730, and of such mortal violence that 10,000 persons died from the scourge.

1744. Cadiz was again afflicted with a visitation of yellow fever, brought into the country by vessels from the Antilles. The extension of the disease was of moderate intensity. The epidemic spread to Majorca, in the Balearic Isles.

1746. At Cadiz a vessel from Cuba again introduced yellow fever.

1749. Another importation took place at Majorca, but the effects were not of much importance.

1753. The squadron of Admiral Don Pedro de la Cerda brought yellow fever to Cadiz. The infection originated in America and was taken to Cartagena by the same ships of war. Happily there was not an extensive spread.

1800. The disastrous epidemic of this year commenced at Cadiz toward the latter days of July. Its first appearance was in the quarter known as Santa Maria and, by August 4, had counted many persons among its victims. The infection spread furiously in the quarters of Ave Maria and San Antonio. Day by day from August on, the pestilence extended, propagating itself through all the neighboring sections of the city. The origin of the contagion was attributed to three sources. Suspicion fell first on the American corvette *Dolphin*, which left Havana, May 27, 1800, for Charleston, where she arrived four days later. From Charleston, the vessel sailed, June 11, for Cadiz, at which port she arrived July 6, 3 of the crew having died of yellow fever on the voyage. Twenty days after the last death and on the completion of ten days of rigid isolation, the health of all aboard being perfect, it was decided to give the corvette free pratique. The second possible origin of the disease was the corvette *Aigle*, which sailed from Havana, May 22, 1800, and on the passage to San Lucar de Borameda lost 5 hands from yellow fever. At San Lucar de Borameda, the crew dispersed and other men were shipped. The *Aigle* arrived at Cadiz June 30, six days after the arrival of the *Dolphin*. A third suspicious source was the ship *Jupiter*, cleared from Vera Cruz, February 4, and arrived at Cadiz, March 28. A few days after her departure from Vera Cruz, 1 of the officers fell ill and died in five days. Then, one after another, all hands aboard were taken sick. The condition of the ship was at one time so desperate that the captain was undecided whether to proceed on the voyage or return to Havana. The members of the crew, however, made a good recovery from their illness, and the vessel went on her way. In addition to the 3 vessels that fell under direct suspicion, it is noted that, a large number of vessels were continually entering the port and that by an order of the King, dated February 1, 1800, it was absolutely prohibited to submit to quarantine any vessel coming from America. Thus all safeguards were for the time removed.

This epidemic was extremely desolating and mortal. Cadiz had at the time a population of 57,499. From August 18 to November 30, the

number of persons who had fallen ill of the disease was 48,520 and of these 7,387 died. At the latter date, there were 357 cases still under treatment. Of those who died, 5,810 were men and 1,577 women. So that of the fatal cases, between 78 and 79 per cent were males. The maximum mortality among males occurred between the ages of 21 and 40, and for females between the ages of 1 and 10 years. The sickness diffused itself in several communities, among others Puerto Santa Maria, Isla de Leon, Puerto Real, Xeres de la Frontera, and finally it reached Seville, August 23.

Seville then had a population of 80,568 inhabitants, of whom 76,685 were attacked by the malady, and 14,685 died. November 30, at the time the statistics were prepared, 85 cases were still ill. The disease appeared in Seville at practically the same time as at Cadiz, perhaps because the destination of the passengers of the corvette *Dolphin* was about equally divided between the two places. It should be remarked that the statistics gathered from a relation of the facts given by the celebrated Dr. Arejulas, who was detailed by the Spanish Government to investigate the disease, differ materially from those contained in a report sent to the Danish Government by Schousboe, consul of Denmark on duty at Cadiz. The two writers are in accord concerning the time and mode of introduction of the sickness, the way it extended and the clinical form it assumed, but differ essentially in statistical figures.

Arejulas' estimates are given in the following table :

Cities.	Popula- tion.	Deaths.	Cities.	Popula- tion.	Deaths.
Cadiz	84,000	16,000	San Lucar.....	18,000	4,000
Isla de Leon.....	32,000	6,000	Rota.....	6,000	1,500
Puerto Real.....	10,000	3,000	Xeres de la Frontera.....	30,000	8,000
Miclana	10,000	(?) 10,000	Seville.....	80,000	30,000
Santa Maria.....	25,000	6,000			

Therefore, in a population of 279,000 there were 77,500 deaths. The disease also invaded Cartagena, assuming grave features and making a shocking slaughter among the inhabitants.

1801. Yellow fever broke out August 3, 1801, in Medina-Sidonia. The first person attacked died in six days. A few days later the relatives of the dead man were stricken, then the malady manifested itself among the inhabitants of neighboring houses, and finally step by step the epidemic spread itself over the entire city.

1802. After the doleful visitation of 1741, yellow fever had spared the city of Malaga at times when it worked its ravages in other cities of southern Spain. But in 1802, Malaga suffered a small epidemic of brief duration.

1803. The slight prevalence of the previous year was like a mild premonition of the terrible calamity that tormented Malaga in 1803. The importation was blamed upon various vessels. A Dutch ship, the

Giovane Nicola, sailed from Smyrna, March 14, and arrived at Malaga on the twenty-second of the same month. During the voyage she had been obliged by contrary weather to take refuge in several ports. Suspicion attached to her. Two French ships were also considered questionable from a sanitary point of view. They were the *Desaix* and *L'Union*, carrying soldiers between Marseille and Santo Domingo and had had deaths of a doubtful nature aboard. The Spanish ship *Providencia* too was viewed askance by the sanitary authorities. She arrived June 9, from Montevideo with dirty documents, tales of yellow fever and, notwithstanding all this, had been submitted to only a brief period of detention. This much, however, is certainly known. The first case of yellow fever was verified in the person of Felix Muñoz, a smuggler, who had gone on board the Dutch ship and returned to Malaga with some pairs of cotton stockings and a quantity of tobacco. Shortly after he sickened of yellow fever and died in five or six days. The municipal sanitary authorities closed the house of the dead man and sent to the open country all those who had been in contact with the patient or who had stopped in the neighboring domiciles. Thirty-six days passed without any case manifesting itself. The disquieting apprehensions of the citizens were therefore calmed for the moment. However, one Christobal Verduras, living in the Perchel quarter, had during this time received another smuggler in his house, where the man was taken ill and died promptly. The facts were for the time concealed and the cadaver transported secretly from the house in the night and buried in the church of San Pedro. August 6, the son of Verduras fell sick, and then his wife and then 3 other sons. In short, within eight days after the death of the second smuggler, 8 persons of Venduras' family were prostrated in the same manner. Three of them died. Afterwards there were cases in the habitations surrounding that of Verduras. At the same time, another center of infection was established where the first smuggler was buried. The parish priest, the pallbearers, the sacristan were attacked, and likewise the physicians who had treated the patient. All of them died. In this way making gradual advances, the whole city was invaded by an intensely pernicious contagion. The epidemic endured until December 18. Of the 48,015 inhabitants that Malaga numbered at the beginning of the outbreak, many fled from the city and carried the scourge throughout southern Spain. The noxious character of the disease is evident from the figures which show that of those who remained in Malaga, 16,517 fell ill and 9,333 died. On December 18 there were still 300 persons convalescent in the hospitals. A fact worthy of remark is the absolute immunity of the large prison in the center of the infection. In the beginning of the pestilence, the commandant of the prison established rigorous isolation and thus seems to have saved those detained in his custody. In the same year, 1803, yellow fever spread widely in the city of Cadiz with great havoc to health and life.

1804. Being unable to fix upon a new source of importation, Spanish epidemiologists concur in the opinion that the renewed prevalence in 1804 was a recrudescence of the scourge of the preceding year. The second attack was for Malaga, at least, more disastrous than the primary invasion. When the first persons were affected in the latter part of June, a wild panic ensued. The inhabitants fled in swarms, so that on July 1 only the poor and needy remained. It appears, however, from the chronicles of the day that this class was sufficiently numerous to furnish ample fuel for the epidemic. It is recorded that, before the close of November, there had been at Malaga 18,582 cases of yellow fever and 7,726 deaths.

Gibraltar, owing probably to the severe measures insisted upon by the local government, had in past years remained free from yellow fever. Presuming upon this fortunate immunity, there was in 1804, from all accounts, a decided relaxation of vigilance. Through the rents in the cordon, several smugglers from Cadiz or Malaga stole into Gibraltar. That they carried something more harmful to public interests than contraband goods is obvious from the sequel. Some of them developed yellow fever in the midst of the healthy population of Gibraltar and died diffusing the contagion among the inhabitants. The epidemic was very deadly, causing a mortality of 4,000 souls.

Cadiz suffered with the other Spanish cities in this year of gloom. The epidemic disease, imported evidently from Malaga, showed a most malignant violence.

Alicante was also fiercely tormented with yellow fever.

At the time of the outbreak at Malaga, a tailor named Delgado, who lived in a house in the Strada Puerta Nueva, escaped from detention and arrived at Antequera July 23. Four days later he was prostrated with yellow fever and died on the sixth day. His father and mother, 3 brothers and 2 sisters lived in the same house. Of these 7 persons, 5 speedily succumbed to the disease. The contagion then spread with incredible swiftness and swept down before it such a number of people that there was not time enough to bury the dead. In the early days of October, the violence was so mortal that between 30 and 37 persons died every day. The populace with religious fervor, hoped, by rendering thanks to God for the preservation of the living, to abate the affliction. A procession was formed with lavish sacramental accompaniments. The ceremony lasted for several hours and was participated in by persons of all classes. The hope of the people seemed, however, to be vain. An augmentation of the epidemic immediately set in and the daily register of deaths ran up to between 80 and 85. November 6 the epidemic was declared ended.

An interesting incident is related as accounting for the outbreak of yellow fever at La Rambla, the same year. A man from La Rambla, moved by religious ardor, was seized with a desire to touch the litter on which the body of a man dead of yellow fever was being borne to the

grave. Returning to his native place, the citizen of La Rambla began to ail from a slight febrile disorder, but was well in a few days. A cousin who had waited on the sick man died of yellow fever a week after. A little later, several other persons who had been in contact with the fever patient fell ill also. Thus several foci of contagion originated at La Rambla, where the disease continued its destruction until November 15.

The epidemic at Mantilla in 1804 was attributed to a monk from Malaga who was taken sick at Mantilla, August 11, and died in five days. The houses where the deaths had occurred were closed and all persons having contact with the cases were isolated. September 4, another monk, a fugitive from Malaga, was attacked with yellow fever and in a few days died. A muleteer returning from Malaga fell victim to the same fate. From these foci, the disease extended to a large portion of the community, but owing, it appears, to the energy of the sanitary authorities did not work such ruin as elsewhere. November 29, the city was declared free from yellow fever.

The city of Espejo is located on a very high level. There arrived, August 27, a muleteer carrying merchandise bought at Malaga. The man fell sick promptly and the physicians diagnosed the case as one of yellow fever. The patient was at once carried into the open country and the goods he had brought were destroyed. All persons who had contact with the muleteer sickened and a majority succumbed. The disease extended at first to the portion of the city frequented by the friends of the muleteer. A rigorous cordon was instituted and thus other sections were spared. The disease terminated November 25.

The prevalent disease was introduced into Vera by a family flying from the rage of the epidemic at Cartagena. Almost all the members of the fugitive family were stricken and died. October 3, an assistant at the hospital was attacked and died the tenth day. From that time on, the malady prevailed in the infected quarter, ceasing in the last days of November, but complete isolation saved the rest of the city.

Ronda, another Spanish city suffered from the scourge of 1804. Two men flying from Malaga took lodgings at Ronda, in the house of a woman of easy morals. The woman died August 4, after an illness of a week's duration. August 12, a neighbor was taken sick and died in two days with the symptoms of yellow fever. All the houses in the neighborhood were then quarantined. This wise police system operated to end the epidemic by the end of October, but not until 50 persons had died of yellow fever.

So far it has been seen that, after nearly half a century of immunity, Spain suffered 5 annual recurrences of yellow fever ending in the year 1804. Then followed a period of freedom from the disease lasting until 1808.

1808. In this year an importation of yellow fever took place at Cadiz, but the developments were unimportant.

The consequences were less happy, however, at Xeres de la Frontera, in which city an individual from Cadiz diffused the contagion. Rigorous prophylactic measures were taken to protect the large prison at Xeres de la Frontera, and were successful until near the decline of the epidemic. At that point some prisoners slipped away, but were captured and returned to the prison. They brought back yellow fever with them, and so terrible was its effects within the prison walls that only a few of the convicts escaped death.

1810. In August of this year an epidemic appeared simultaneously in Gibraltar, Cadiz, and Seville. It was impossible to determine definitely where the disease began, but it seemed probable that it was introduced into Cadiz and Seville by smugglers. Its maximum prevalence was at Gibraltar. The epidemic was also transplanted in Cartagena and attained considerable violence.

1811, 1812. At Cartagena, the disease appeared again in the 2 following years and, inasmuch as no new source of importation could be discovered, the epidemics of 1811 and 1812 were considered to be a reawakening of the pestilence of 1810.

1813, 1814. In these years there was yellow fever at Gibraltar, the first year from an original importation, the following year from a revival of the contagion introduced the previous summer.

1819. Spain had enjoyed five years' exemption from yellow fever when a period of deadly pestilence arrived. Cadiz was doomed to suffer one of the most widespread and mortal epidemics that ever fell to her fate. The King of Spain prepared a military expedition to go to the Americas and, among other vessels, hired a ship named *San Juliano*, recently returned from the Philippine Islands. The vessel had scarcely begun to take her cargo of cannon powder at the Isla de Leon when suspected cases of yellow fever appeared among the persons employed aboard. The disease broke out also in the quarter of the city called Barrio del Christo where the baggage of the crew of the *San Juliano* was deposited. The persons taken sick all died and very quickly too. This occasioned great alarm in Cadiz and the commandant of the city sent his chief sanitary officer, Dr. Flores, to Isla de Leon to study the disease and report on its nature. Dr. Flores, convinced from his investigations that the disease was yellow fever, declared that rigorous measures alone could avert a disaster. But his counsels were not listened to. On the contrary, he was accused of high treason and held for trial before a tribunal of war. The commanding general assured the alarmed population that yellow fever did not exist on the Isla de Leon, and boastfully added the rather unintelligible information, that should it enter the city of Cadiz, he was prepared to meet it with the point of his sword. Notwithstanding all assurances to the contrary, the unheeded warning of the unfortunate Flores came true. The scourge struck with frightful force, and among the first to run away from the city was the redoubtable general.

From July to December, when the epidemic ended, there were 40,000 cases and 8,000 deaths in Cadiz.

A woman who fled from Cadiz took refuge in Seville and died there from yellow fever. From this focus the disease extended throughout the city, manifesting the same violence and malignancy that it had shown at Cadiz.

The epidemic also entered Xeres de la Frontera, where it was highly mortal in its effects.

1821. The story of the fatal diffusion of yellow fever at Barcelona in 1821 is one of the most dismal in the sanitary history of Spain. In the port were anchored many vessels of all nations, among them the *Tailla Piedra* and the *Gran Turco*, recently arrived from Havana. A great festival was arranged for July 12, to celebrate the anniversary of the promulgation of constitutional law in Spain. Bad weather prevented the feast being celebrated in the harbor, and the festivities were therefore postponed until July 15, the following Sunday. On Sunday the weather was splendid and a large concourse of people congregated to witness the fine spectacle. Captain Sagredas, commanding the *Gran Turco*, gave a reception on board his ship. His wife, their children, and many other persons, altogether 40, attended. Later, the whole party paid a visit to the *Tailla Piedra*. After spending a couple of days aboard the *Gran Turco*, the captain's family went to Barcello. netta, where they lived. In a few days every member of the family sickened of a strange malady, and all died. A like fate befell most of the other persons who visited the *Tailla Piedra*. Of the 40 persons, 35 died.

Near these ships, the French brig *Josephine* was riding at anchor. The crew was taken with yellow fever and few survived. There were suspicious cases, too, on board a war ship of the Kingdom of Naples. They were at first attributed to food poisoning from using for culinary purposes a badly tinned copper vessel. The captain of the *Josephine* took lodgings ashore at Barcelona. Eight days afterwards, the woman who kept the inn, where he stopped, was attacked by yellow fever, and in rapid succession her husband, their children, and the servants fell ill. The disease reached out into the neighborhood, extending in a short time to the whole quarter, and later overspread the city of Barcelona. The municipal authorities adopted proper sanitary measures at the outset, but they met with great opposition from the people who objected to interference with their business and pleasure, and foolishly refused to regard the situation seriously until the epidemic had gained the upper hand. The maximum intensity of the prevalence was in September. The Report of the National Academy of Barcelona, says:

It is impossible to know positively the number of victims carried off by the epidemic that covered Catalonia with mourning, nor to state the number of those that died in the neighboring country or that gave up their lives at Mahon, Tortosa, and Mequinenza.

Francois (in his report to the French Government), Mazet, Pariset, Bally, and Auduard agree in estimating that approximately in the city of

Barcelona, during the five months that the epidemic raged, 25,000 persons died. Of the population of 150,000, about 80,000 fled from the city.

The same year, 1821, a Danish brig, the *Initium*, sailed from Barcelona and in six days reached Malaga. On the voyage 4 of the seamen were sick with yellow fever, and 1 died at sea. Arriving, the brig was committed to the lazaretto. After a period in quarantine, she was given free pratique and took two additional hands aboard. These new men promptly sickened of yellow fever, and both of them died. Suspicious cases appeared on some English, Danish, and Dutch vessels that were anchored alongside the *Initium*. At the beginning, the sickness was confined to the vessels in the harbor, but early in September a master calker, who had been working on one of the ships, carried home with him some effects that had been aboard. September 7, his son was taken ill and died. Then he himself fell sick, but recovered. Other cases broke out on the same street; other quarters became infected, and so the disease diffused itself over the city.

The city of Tortosa had never suffered from an invasion of yellow fever, even at times when the disease was most widespread in Spain. In the night of August 5, the ship *Madona de la Cinta*, coming from Barcelona, entered the port of Tortosa and set ashore a seaman and a soap maker. Both of them died shortly of yellow fever. The seaman died in the country and the soap maker at the house of a soap manufacturer. The latter and his family were stricken with the disease. Then the doctor and the priest fell ill. In this manner the disease invaded the city. The form of infection from all reports was extremely fatal, for it is recorded that all the physicians, pharmacists, priests, monks, and nuns in the city died. After a month's time only 5,000 persons remained in Tortosa. Ten thousand persons fled, and at the end of the epidemic 4,500 of the 5,000 that remained were dead of yellow fever.

AlSCO, a city situated on an elevated site about 30 kilometers from Tortosa, was taken with yellow fever and almost decimated. A citizen of Tortosa while in AlSCO learned that his wife was ill in Tortosa. He borrowed a horse from a friend and hastened to join his wife. Both man and wife died. The owner of the horse wanted his animal back, so he sent a servant to Tortosa to fetch it. The servant brought back the horse, but died of yellow fever and infected AlSCO.

Meguinenza also suffered an importation of the pestilence through the medium of a vessel from Tortosa which arrived August 28. A sailor was taken ill soon after disembarking and died August 30. Other members of the family died in a few days, and finally the malady affected a large portion of the community, producing disastrous results.

Palma, the capital of the Balearic Isles, paid tribute also to yellow fever in 1821. A vessel bound from Barcelona to Majorca carried on board a merchant of Palma as a passenger. Arriving home the merchant was attacked with yellow fever, but recovered. Two days later, his little daughter was taken ill and died. From this focus, the disease

was disseminated, attaining the proportions of a great epidemic that destroyed half the population of Palma.

The frightful fierceness of the epidemic of 1821 in Spain, and the havoc produced in the wealth and life of the richest industrial section of the peninsula by frequently repeated and devastating pestilences, attracted the attention of other nations. There were accusations of negligence in the enforcement of sanitary regulations. This led the Government of Spain to adopt precautions for the prevention of future disasters. The leading academies and societies of medicine in the Kingdom were interpellated as to whether yellow fever could be considered absolutely of American origin and of an infectious and contagious nature. With several opinions to the contrary, the majority were convinced of the exotic origin of the disease and that it was infectious and contagious. As a consequence, stringent provisions of maritime sanitation were devised and put into effect.

1823. In this year the little port of El Passaje, situated on the north coast of Spain, was infected with yellow fever by the Spanish brig *Donastierra*, from Havana. The authorities sank the infected ship. There were only a few cases ashore.

1829. Two ships, the *Dydden* and the *Neta*, arrived at Gibraltar, having yellow fever aboard. Linen soiled with vomited matter was sent, part to a laundry in Gibraltar, part to a laundry in the village of Catalan Bay. The washerwomen contracted yellow fever and died. The infection was circumscribed and not very violent.

1870. After over forty years' immunity, Spain again found yellow fever within her borders. Early in August, 1870, the ship *Maria* arrived at Barcelona from Havana having yellow fever aboard. Through some irregularity, it is stated, the vessel was given free pratique without being required to undergo the necessary sanitary treatment. The physician of the port and the secretary of the sanitary office were blamed for the importation. They were both taken with the yellow fever and died. Other members of the same families were stricken and then some persons who had been in direct contact with the sick and with their effects. The disease spread through the city. During the months of August and September the mortality reached its maximum. Toward the middle of October the daily mortality varied from 25 to 40.

The disease extended rapidly to Valencia, Alicante, and Palma and was taken by refugees to Madrid. There were only a few cases in the capital.

1878. The history of yellow fever in Spain ends with an epidemic at Madrid in 1878. A body of soldiers from Havana was disembarked at Santander and transported by rail to the capital city. They had scarcely arrived in barracks when yellow fever broke out attacking 50 soldiers, of whom 30 died. All the soldiers who fell sick had come with the party from Havana. The disease was not communicated to the other persons who were in attendance on the sick.

YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN No. 6.

Section C.—TRANSMISSION.

Surg. J. H. WHITE, Chairman of Section.

A NOTE ON MOSQUITOES IN BAGGAGE.

By S. B. GRUBBS, *Assistant Surgeon, M. H. S.*

(Experimental Investigation in Hygenic Laboratory, M. H. S.)

MARCH, 1902.

A NOTE ON MOSQUITOES IN BAGGAGE.

In the light of recent well-known work, showing that the infection of yellow fever may be transmitted by certain mosquitoes biting a person suffering from that disease, and, after a certain lapse of time stinging a nonimmune person, and on account of the modifications in the methods of preventing the spread of this disease proposed on account of this discovery, enormous sanitary and quarantine interest attaches to the question, How far may a mosquito be carried in baggage?

That these insects may be harbored for weeks in vessels and railroad trains, and even breed in enormous quantities in the water tanks of ships, and so be carried almost any distance, has been shown in many instances. Howard considers the railroad one of the principal means of spreading this pest, and instances are numerous of out-of-the-way villages or localities, previously free, being infested with mosquitoes after getting railroad connections (a).

Interesting instances of mosquitoes being carried great distances at sea were reported lately in the public health reports. Passed Assistant Surgeon Cumming stated that the Spanish bark *Maria Blanquer*, sixty-five days from Rio de Janeiro, arrived at South Atlantic Quarantine Station carrying a veritable plague of mosquitoes, most all of which were the

(a) Howard, "Notes on the mosquitoes of the United States," and one instance personally known to the writer.

were ruined by the growth of molds, but boxes were found having one or more alive on the second, fifth, seventh, and eighth days.

By the word damp it must not be understood that a factor of moisture was introduced greater than could be found in actual packed clothing. In most of the experiments and in all of those cited, the wet towel or piece of fabric to be wrapped about the box was wrung out by hand as much as possible and then folded in a dry towel and the wringing repeated. This would leave it a little damper than freshly ironed linen, or the filthy sweaty clothing so often found by those engaged in practical disinfection.

As before stated, all these experiments were made on mosquitoes confined in circular pill boxes, one side of which had been replaced by gauze. Their arrangement prevented their being crushed in the packing and manipulations, but also introduced two features that would tend to shorten their lives, viz, first, the violence done in getting them into a small box, and, second, the restraint that prevented them from themselves seeking the conditions best favoring their survival. This ability of the mosquito to protect itself is very pronounced and has been noticed in the experiments made on them with gaseous disinfectants. (Laboratory Bulletin No. 6.) It would probably play a rôle in prolonging its life under natural conditions.

Disregarding these unnatural conditions, we must conclude from our observations on the *Culex pungens* that mosquitoes having once found their way into trunks, boxes, bundles, or other baggage could live there at least five days, ample time to carry them from the infected ports of Mexico or Cuba to any of our Southern ports. It is true the vast majority of the *Stegomyia fasciata* so carried would probably not be infected, but even these could by their propagation render infectible a locality previously immune.

Some eminent authorities, speaking from a practical standpoint, have opposed this view. Reed, of the United States Army Commission, in an address on "The Prevention of Yellow Fever," read at the twenty-ninth annual meeting of the American Public Health Association at Buffalo, said:

The fear that has been entertained that infected insects may be imported in boxes or trunks we believe to be absolutely groundless, and this for the simple reason, as shown by numerous observations made by us, that mosquitoes, when deprived of water, die within a few days. Even if allowed to fill themselves with blood immediately before the experiment is begun and then deprived of water, practically all are dead by the expiration of the fifth or commencement of the sixth day. We may say that of a large number of insects tried in this way only 1 female has survived until the sixth day, and then in a feeble condition. Males and females which have been living on sugar and water, or fed two days before on blood, if deprived of water and food, begin to die after twenty-four hours, and all are dead on the fourth morning. Free access to water, therefore, is necessary for the existence of this mosquito.

As will be seen the above view is in accord with our observation that mosquitoes kept exposed to ordinary conditions or in dry wrappings

die in two or three days. However, this does not consider the factor of moisture except as water. The effect that a very slight amount of moisture will have on the length of time this insect will live is really remarkable. A mosquito that has entered a piece of baggage would never have free access to water, but it could often find the small amount of moisture necessary for its existence, and it could besides find protection from atmospheric conditions, for, as we have remarked, our confined mosquitoes live longer if wrapped even in a perfectly dry cloth than when entirely exposed.

Surg. H. R. Carter, of the Marine-Hospital Service, whose painstaking and extensive observations are well known, writes:

For the twenty years preceding 1899 the baggage from Vera Cruz, Havana, and Santiago de Cuba, on vessels arriving at New York, unless with yellow fever en route, entered without disinfection. The amount of this baggage from Havana and Vera Cruz is large, and it is not possible but that much of it came from houses infected with yellow fever and much of it was not clean. All of this baggage was opened at the custom-house at New York and handled in hotels there and at Saratoga, and no yellow fever is reported among the customs inspectors in New York, or at the hotels during this time.

The baggage going from the same ports to Spain for the last thirty years is even more to be considered. Its amount has been enormous; much of it (from the class of people to whom it belongs) must have been foul. Some, the lesser part, it is true, of this traffic goes to the Mediterranean ports of Spain—Valencia, Malaga, and Barcelona, etc.—which at times, 1870 and before, have been “infectible places,” yet, I think, we have had no yellow fever reported in the Peninsula since the epidemic of 1870.

Of course, negative evidence is convincing only in proportion to its mass, and that a piece of baggage or 100 pieces of baggage from an infected place did not convey infection to nonimmunes exposed to it, means little, yet the amount of this baggage is so large—I can not estimate it at less than that of 300,000 persons from Havana alone—that we must claim that a very large number of pieces of baggage from infected houses have been introduced into New York and Spanish towns, that numbers of susceptible people have thus been exposed under various conditions, but have not contracted yellow fever.

To me the mass of this evidence is sufficient to be convincing, and I count it proven that baggage from Havana and Vera Cruz will not convey yellow fever directly to people after the voyage to New York or Spain, thus that yellow fever is not conveyed by mosquitoes carried in such baggage.

Whether this time element is necessary, of course, is not determined by these observations, but it is a factor in them.

Whether the rare cases of yellow fever we sometimes see contracted from infection aboard ship may be due to infected mosquitoes brought aboard in the hand baggage of passengers, and opened soon after coming aboard, may be a question. The sister who developed yellow fever aboard the *Vigilancia*, en route from New York to Havana, is a case in point, and we occasionally see members of the crew with yellow fever. One occurred in Havana harbor on a Ward liner en route from Vera Cruz to New York in 1900. Other explanations of these cases may, of course, be possible.

It is equally true that yellow fever has frequently been conveyed by ships on which no yellow fever exists, and not unfrequently by vessels on which we can get no history of there having been any yellow fever. In these cases there are doubtless mosquitoes already infected in the hold or other parts of the vessel, to which the crew have not been exposed since they became capable of transmitting the disease; or the crew may have been immune to the disease.

Thus looking fairly at both sides of the question and reviewing the experiments and observations that have been presented, it would seem that it is entirely possible for a mosquito to enter ordinary baggage and live there long enough to be carried from the infected ports within a few days sail of our Southern shores, but that in reality they are seldom so carried. Further observation by our quarantine officers and others alive to the subject is needed before final judgment is passed, and the object of this note is to stimulate such work on this important subject.

YELLOW FEVER INSTITUTE,

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN No. 7.

Section D.—QUARANTINE AND TREATMENT.

Surg. R. M. WOODWARD, Chairman of Section.

YELLOW FEVER—ITS OCCURRENCE AND QUARANTINE MANAGEMENT AT THE PORT OF MARSEILLE, FRANCE.

FROM REPORT OF THE CONSUL-GENERAL OF THE UNITED STATES AT MARSEILLE,
FRANCE, TO THE DEPARTMENT OF STATE.

MARCH, 1902.

CONSULATE-GENERAL OF THE UNITED STATES,

Marseille, France, January 2, 1902.

SIR: I have the honor to inclose, for transmission to the United States Marine-Hospital Service, a report on the subject of yellow fever at Marseille, as instructed by the Department's circular of December 5, 1901.

I am, etc.,

ROBERT P. SKINNER,
Consul-General.

Hon. DAVID J. HILL,
Assistant Secretary of State.

YELLOW FEVER AT MARSEILLE.

Very little information is obtainable at Marseille concerning the subjects mentioned in the Department's circular of December 5. Thus far, France has escaped any serious epidemic from this cause. In 1821, Barcelona passed through a rather severe experience, and in 1857 Nantes was similarly afflicted, although but 7 deaths were reported at that time. In both instances, the disease was imported. The city of Marseille, properly speaking, has been absolutely exempt from cases of yellow fever, although on the quarantine island of Frioul it is not entirely unknown. The attitude of the Government with respect to this malady is fully set forth in article 61 of the quarantine law.

In France, from November 1 to February 20, if a ship arrives from a port contaminated with yellow fever, whether said ship be above suspicion, suspected, or infected, the authorities will limit themselves to a medical visit among all the passengers, the disinfection of all soiled linen and similar apparel, and bed clothing, and other suspected articles contained in passengers' baggage, and the disinfection of the ship or of the part

of the ship which the sanitary authorities may judge to be contaminated. If cases of yellow fever are found on board said ships, they will be immediately removed and isolated until their cure; the other passengers and the crew will be subjected to surveillance (as ordered by article 57), for seven days.

The happy exemption of this country from yellow fever causes the authorities to feel that there is practically no danger of serious epidemic from this source. Dr. Catelan, the chief of the quarantine, has long since been convinced of the danger of infection from mosquitoes, and his first care, so he tells me, upon the landing of cases at the island of Frioul, is to arrange mosquito nettings about the bed of the patient in such manner as to prevent the local mosquitoes from spreading the germs. I append herewith a list of the ships arriving with cases of yellow fever on board during the last ten years and other statistical information in relation thereto.

While the French Government is undisturbed with respect to the possibilities of yellow fever in this country, the ravages wrought by the disease in Senegal and other of the French colonies have awakened the medical authorities to the importance of the subject, and a commission of scientific men has recently been sent out from Paris on a mission of investigation. They have already visited Senegal, and are supposed to be en route for Brazil at this time. For many years the annual epidemics in Senegal were supposed to arise from unpreventable causes, and true yellow fever was not identified as such until comparatively recent times. The ravages are so severe in that colony that upon the outbreak of fever immediate efforts are made to deport all Europeans engaged there in business or in the Government offices. This radical action necessarily disturbs business, and the medical authorities are hopeful of finding some means of counteracting the plague.

ROBERT P. SKINNER,
Consul-General.

List of ships arrived at Frioul, infected with yellow fever, from 1891 to 1901.

Date.	Name of ship.	Nationality.	Port of departure.	Duration of passengers' isolation.	Number of passengers disembarked.	Cases and deaths during voyage.		Number in lazaret.	
						Cases.	Deaths.	Cases.	Deaths.
May 17, 1891	Béarn.....	French...	Plata.....	<i>Days.</i> 10	665	0	5	5	a 1
Jan. 19, 1892	Chérifon	do.....	Santos.....	3	103	0	2	0	0
Apr. 14, 1894	Espagne.....	do.....	Buenos Ayres and Rio Bahía.	4	336	2	1	0	0
Apr. 17, 1898	Provence	do.....	Brazil	5	416	8	4	0	0
May 3, 1898	Les Andes	do.....	do.....			2	1	0	b 0
May 11, 1898	Colombo.....	Italian...	do.....			0	2	0	c 0
Nov. 3, 1899	Aquitaine.....	French...	Buenos Ayres.	3		1	1	1	d 0
Aug. 18, 1900	Vauban.....	do.....	Rufisque...	7	5	3	2	0	0
Total.....								6	1

a Four cured.

b Passengers remained on board.

c Left port same day for Genoa.

d Women entered at Frioul hospital on eighth day, had lost 2 children during voyage.

YELLOW FEVER INSTITUTE, BULLETIN No. 8.

Treasury Department, U. S. Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

YELLOW FEVER

IN

France, Italy, Great Britain, and Austria

AND

BIBLIOGRAPHY OF YELLOW FEVER IN EUROPE.

MAY, 1902.

WASHINGTON:
GOVERNMENT PRINTING OFFICE.
1902.

YELLOW FEVER INSTITUTE.

Treasury Department, U. S. Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN No. 8.

Section A.—HISTORY AND STATISTICS.

Surz. GEORGE T. VAUGHAN, Chairman of Section.

YELLOW FEVER IN FRANCE, ITALY, GREAT BRITAIN, AND AUSTRIA, AND BIBLIOGRAPHY OF YELLOW FEVER IN EUROPE.

By J. M. EAGER, *Passed Assistant Surgeon, M. H. S.*

MAY, 1902.

YELLOW FEVER IN FRANCE.

In a history by Arcere of the city of La Rochelle, published in 1756 (vol. 2, chap. 4, cited by Frank), there is a reference to an importation of yellow fever that occurred at La Rochelle toward the middle of the year 1700. The report, however, lacks proper corroboration.

1802. In the autumn of 1802, there arrived in the roads at Brest a squadron of 5 vessels of the line commanded by Admiral Villaret de Joyeuse. The ships had come from Santo Domingo. Among the crews were 42 persons in the active stages of yellow fever and many convalescents. The sick seamen were disembarked at the lazaretto of Tiberon, where 32 died. A custom-house official, after being for several days on duty aboard one of the vessels, the *Tourville*, was taken with yellow fever. He died at his home ashore. Fortunately, some of the medical practitioners who were called in to see the sick man had been in the West Indies. Thus the case was recognized as one of yellow fever. Strict sanitary measures were adopted and, probably owing to these precautions and the fact that the season was advanced, the disease did not spread.

The American ship *Columbia* arrived at Marseille in 1802 with yellow fever aboard, but there was no diffusion ashore.

1821. In this year there was an epidemic of yellow fever in Spain. Several vessels that had had yellow fever aboard on the passage from Barcelona entered the port of Marseille. All were remanded to the lazaretto. A carpenter who worked at the lazaretto died in a hospital at Marseille. Another case occurred in a hospital at Marseille that year in the person of a sailor who had come from Barcelona by land. The disease did not spread. The mayor of the city, with a view to averting an epidemic, sent for the famous professor Palloni, who had been through the yellow-fever epidemic at Leghorn in 1804, and whose diagnosis and advice were relied and acted upon at Marseille with the happy results mentioned.

1839. The corvette *Caravane* arrived at Brest with yellow fever aboard. During the voyage 116 members of the crew had been down with yellow fever and 33 died. No cases occurred ashore.

1861. In the year 1861 there occurred at Saint Nazaire the only important epidemic of yellow fever that ever broke out in France. In an article on mosquitoes and yellow fever, published in Paris last year (1901), De Gouvea concludes that the epidemic at Saint Nazaire, so carefully observed and recorded by Melier, was determined by mosquitoes infected at Havana and transplanted to France in the hold of a vessel.

The *Anne-Marie*, a ship of the port of Nantes, with a crew of 16 souls, sailed from Havana June 13. The vessel carried barrels of sugar, between the tiers of which layers of sugar cane were placed, in order to properly dress the cargo. After five days' navigation, five days of broiling calms and storms followed by rains, the captain, in order to rest the crew, decided to drift in the Strait of Florida without using sails. Passing out of the strait, the winds became steady, and the men went to work with a will to make sail, showing no trace of fatigue or malady. July 1, namely, eighteen days after the departure from Havana, 2 seamen fell sick, and died within a few hours of each other on the fifth day of their illness. July 2, another sailor was taken ill, but it is recorded that "with strong doses of the sulphate of quinine and with violent purgatives, he was cured after ten days." On successive days, 6 other persons were stricken, including the captain. All were dosed with quinine and cathartics and recovered more or less promptly. Altogether, among the 16 persons aboard, there were 9 cases of sickness and 2 deaths. In this condition the ship entered the port of Saint Nazaire, twenty days after the last death and ten days after the inception of the final case of suspicious illness. Since no case of sickness had occurred during the last ten days and all were well on board at the time of arrival, the vessel was punctually given pratique, in conformity with the French sanitary regulations.

The *Anne-Marie* lay near the shore, not far from the railroad. At her side were 2 other vessels, the *Chastang*, belonging at Indred, and the *Cormoran*, of the imperial navy. The latter vessel was loading

boilers from the former. The crew of the *Anne-Marie* was disbanded and the captain, who had not yet recovered robust health after his recent illness, went to Paimboeuf to recuperate. The discharge of the cargo was entrusted to 17 stevedores, all hale and hearty men.

From July 25 to July 29 the *Chastang* lay near the *Anne-Marie*. Some of the men of the *Chastang* went aboard the *Anne-Marie* and paid a visit of a quarter of an hour's duration. July 29, the *Chastang*, with a crew of 5 men, left for Indret, a place 25 miles above Saint Nazaire. They arrived at Indret the same day. A mechanic on the *Chastang* sickened August 1 and died in four days. At about the time of the mechanic's death 3 men of the crew of the *Chastang* were taken with the same symptoms. The clinical picture was that of yellow fever. The news of what had occurred at Indret had not yet reached Saint Nazaire when, August 2, the first officer of the *Anne-Marie*, a robust man, aged 28 years, died after being ill of yellow fever for sixty hours. The next day, a cooper, who had spent several days in the hold of the *Anne-Marie* engaged in repairing sugar barrels, fell sick of the same disease and died in five days. August 4, a master stonecutter, who worked on the harbor front, 260 meters from where the infected vessel was stationed, acquired the disease, and after six days died. He had had no communication with the ship, no contact with the men or merchandise of the vessel. August 5, 5 stevedores from the infected ship were attacked. Three died in about four days, the other in eight days. August 7, there were 3 more cases, and 2 others the following day. A woman who sold old clothes, sails, and cord was taken sick of yellow fever August 6. She had received in her house 2 seamen of the *Anne-Marie* and had bought from them some discarded garments and odds and ends of canvas and cordage. The next day, a prostitute, aged 55, who had intimate relations with the stevedores of the pest ship, was prostrated with the same malady. A laborer, engaged in handling the cargo of the *Anne-Marie*, lived with a cobbler at a long distance from the port. The cobbler, who sat at his bench from morning till night and never moved from the place of his work, was stricken with yellow fever and died in a few hours. His guest, the laborer, and the laborer's wife both took the disease, but got well.

The *Cormoran*, with 6 men in the crew, was for four days (July 31 to August 3) near the *Anne-Marie*, loading boilers, as has already been mentioned, from the *Chastang*. The *Cormoran* had no communication with the *Anne-Marie*, and it is explicitly stated that she was exposed only to the emanations that issued from the ballast of the infected vessel during the discharge of cargo. The *Cormoran* went to Lorient, a place near Saint Nazaire, August 10. Four days later, 2 of her crew showed symptoms of yellow fever and were dead in forty-eight hours. The necropsy confirmed the diagnosis. Two lighters were also anchored near the *Anne-Marie*. One, the *Jean Bart*, had a crew of 2 men; aboard the other, *Pere Eugraud*, were 2 men and a woman. A man of the crew

of 1 of the lighters had been on the *Anne-Marie* for a few minutes only, but some of the lightermen had assisted at the funerals of the victims at Indret. All the 5 persons on the lighters suffered from a disorder which, though it had not the typical characteristics of yellow fever, bore a close resemblance to the milder form of the disease.

Still other vessels were infected from the *Anne-Marie*. A steamer that ran between Saint Nazaire and Lorient, known as *No. 6*, was for two days (July 28 and July 30) alongside the *Anne-Marie* and had communication with the stevedores. *No. 6* left Saint Nazaire July 30. During the trip to Lorient 1 of the stokers fell ill. He died in six days. About the same time the ship's boy took the same disease, but recovered.

A three-master, the *Dardanelles*, lay side by side with the *Anne-Marie*, August 2 and August 3, in such a position that to go ashore from the first it was necessary to cross under cover of the second. The ship's boy of the *Dardanelles* suffered a typical attack of yellow fever, but did not die.

A vessel from Marseille had been anchored in the harbor of Saint Nazaire from June 23. In order to prepare for her departure she was put alongside the *Anne-Marie* exactly in the position previously occupied by the *Dardanelles*. This vessel, after her departure, spent two days at Belle Isle. She then went to sea and lost her second officer from yellow fever. The officer fell sick August 5 and died after seven days. Twelve days after his death the ship's boy presented the same symptoms, including black vomit, and died in nine days. On the 26th the apprentice developed the disease, but recovered. August 29 a seaman took to his bunk with the malady; September 11 the captain sickened. During the next month 6 other men were prostrated by the disease. One of them died on the fifth day after invasion, the others recovered.

Altogether, the *Anne-Marie* infected 7 vessels, on which there were 40 cases of yellow fever and 23 deaths.

At Montoir a doctor named Chaillon was taken sick with yellow fever and died in four days. He had been in attendance on a patient who had worked as stevedore on the *Anne-Marie*.

The records of the epidemic at Saint Nazaire show that all the infected ships were stationed down the wind from the *Anne-Marie*. The fact is established by the data of the meteorological and maritime observer at Lorient. It is interesting to note that a ship of the imperial navy, the *Chandernagor*, and a passenger transport, the *Lorientais No. 3*, posted near the *Anne-Marie* but up the wind, were perfectly immune from yellow fever. The distance of anchorage and the length of time passed near the infected vessel seemed to have had decided influence in determining outbreaks of the disease. The prevailing temperature did not appear to have any influence. The daily temperature during the epidemic oscillated between the maxima of 21° and 25.5° C. and the minima of 11.8° and 17° C.

H. de Gouvea, in his article already referred to on mosquitoes and

yellow fever, published October 12, 1901, in *Le Bulletin Medical, Paris*, referring to the epidemic just described, says:

All these facts adapt themselves in a perfect fashion, in our opinion, to the theory of the propagation of yellow fever by mosquitoes. We may assume at the outset that, during the loading of the vessel at Havana, a certain number of mosquitoes, previously infected by sucking the blood of yellow-fever patients living in the near neighborhood, could enter the vessel's hold filled with cases of sugar and many stalks of sugar cane placed as a filling in the angular spaces of stowage to hold the cases in place and prevent friction. The stalks could have furnished the mosquitoes with necessary nourishment during the voyage.

During the broiling calms that followed five days after the departure of the vessel from Havana, the mosquitoes, excited by the heat of the atmosphere and of the hold, could very easily pass the defective bulkhead that separated the hold from the lodgment of a certain number of the crew and installing themselves in that place sting the sailors who, as we have seen, were at the time enjoying a period of repose, and thus inoculate them with the germs of the disease. The infection of the stonecutter who was at a great distance (260 meters) from the vessel, and who had had no contact with the ship, is explained in the present state of our knowledge in the following way: The infected mosquitoes escaping from the hold of the vessel and carried by the wind that blew in the direction of the workman, fixed themselves upon and stung him. The infection of the physician of Montoir, Dr. Chaillon, is explained in the same manner by the stings that he had received during his prolonged visit to the patient whom he treated, a stevedore of the *Anne-Marie*, suffering from yellow fever and living in a room on the ground floor in a marshy region where paludal fevers prevailed.

All the other cases of infection are explained very simply since they all occurred in individuals who had been for a longer or shorter time in the hold of the vessel or in individuals who, like the sailors of the other vessels, had been down the wind from the infected ship. With all the cases of yellow fever that occurred at Saint Nazaire and Montoir, the malady was not propagated by any of the effects of the crew, taken with them to their families nor by the ship's cargo sent directly to Nantes by the railroad.

Following the epidemic at Saint Nazaire there were reports of the importation of yellow fever in many of the ports of France, not only Mediterranean, but those of the west and north as well. There was, however, no diffusion of the disease.

1862. A vessel named the *Harriet* arrived, in the year 1862, at Havre with yellow fever aboard. The cases were so numerous that the authorities were forced to open the lazaretto at Tatihon, near Cherbourg.

1870. At the time of the epidemic in Spain, a vessel named the *Argos* arrived at Marseille from Barcelona with yellow fever aboard. The cases were all cared for in the lazaretto, except 1 seaman, who went to Marseille by land, was attacked by yellow fever, and died in the municipal hospital. Fortunately, there was no spread of the disease.

YELLOW FEVER IN ITALY.

The history of the two epidemics in Italy alleged to have been yellow fever, namely, those at Leghorn in 1804 and at Torre Annunziata in 1883, are of interest because of the heated discussions that arose as to diagnosis and the strenuous opposition that was made against branding the affected communities with the name of yellow fever, conditions

recalling the story of many an epidemic that has prevailed in various localities in the United States. The diagnosis in these two epidemics was so obscured by controversy that it will always be open to question. It depends upon the relative value that the student of their history places on the documentary evidence left by the physicians and public officers who had to deal with the disease.

1804. A Spanish ship, the *Anna Maria*, entered the port of Leghorn, August 18, 1804. On a voyage from Havana to Cadiz this vessel had lost almost the entire crew from yellow fever. At Cadiz the ship was refused permission to enter port, but was allowed to recruit the crew in quarantine. Through some irregularity the *Anna Maria* was given clean papers at Cadiz and, July 10, passed Gibraltar and proceeded to Alicante, where she received free pratique. The vessel sailed from Alicante August 9, and reached Leghorn August 18. Owing to the prevalence of yellow fever in Spain, special sanitary restrictions had, since July 17, been placed on all vessels arriving at Leghorn from Spanish ports. There had been sickness on board the *Anna Maria* on the passage from Alicante to Leghorn. The declaration of the captain, supported by oath, and the liberal donations of money made by the owner of the cargo, appear to have been effective in quieting all apprehensions at Leghorn. The ship was given free pratique. Two sick men taken from aboard were carried ashore and lodged at an inn in the Strada Pescheria Vecchia. These men died three days after, and a few days later 12 persons at the inn were taken sick. All the cases ended fatally. A Neapolitan who had left the inn at the first appearance of the disease was attacked ten days after and died in another neighborhood. A French butcher who took breakfast at the inn in the Strada Pescheria Vecchia died of the disease in ten days. Soon after his wife, the woman who owned the house in which he lived, and a friend, an officer of the French army, died of the same affection. At the time these events were occurring at the inn, another focus was formed at a bakery in the Via San Antonio. A baker had brought from the infected ship a quantity of sacks which were to be filled with biscuits. The bread was baked in the night and, in the intervals between ovenfuls, the bakers rested themselves by lying down on the empty bags. In a few days these men were stricken with a strange malady. Suspicion was directed against the *Anna Maria* as the source of the disease, and sanitary guards were stationed aboard. In their turn, the guards acquired the disease.

The cargo of the *Anna Maria* consisted of sugar, hides, and wood used in the art of dyeing, and was stored in warehouses in different parts of the city. In the neighborhood of these magazines the disease gained quick headway. The porters who handled the goods and the custodians of the warehouses were taken with the disease. Two porters and 1 custodian died. Thus, spreading by degrees, the malady extended throughout the city of Leghorn. At that period Leghorn had a popula-

tion of 60,000, not counting the men of the French garrison. About 7,000 inhabitants fled to Pisa. The French soldiers were transferred elsewhere. None of these persons who left the city carried the disease to their new residence.

Two French physicians, Lacoste and Dufour, made a study of the malady. Lacoste had been for many years a medical officer of the army in the French Antilles. Dufour was a sanitary official of Leghorn and had conducted many necropsies. Lacoste and Dufour made post-mortem examinations of the bodies of the French butcher and the officer of the French army. As to their diagnosis, they only reported that the men died of a contagious disease. They did not assign to the disease the name of yellow fever.

After the flight of the 7,000 persons to Pisa, a sanitary cordon was thrown about Leghorn, thus cutting the city off from the rest of Tuscany. In October, the government of Tuscany sent to Leghorn a commission composed of the celebrated Professor Palloni and Drs. Bruni and Bertini. The figures showing the ravages of this epidemic are very conflicting. Lacoste says that 1,900 persons died during the epidemic, Coppie says 1,500, and Palloni 700. These discrepancies can be readily understood when account is taken of the state of panic that prevailed and the confusion that invaded the families of the sick or dead when they were turned out of their houses and the habitations burned to the ground. According to the reports of Palloni, there were 7 deaths in August, 51 in September, 204 in October, 390 in November, and 3 in December.

The government commission was composed of men of experience and learning; who studied the epidemic thoroughly and suggested the wisest measures of sanitation. But it is a curious fact that when it came to defining the malady they remained mute. The only conclusion that can be drawn is that silence on this point was a condition imposed upon them by their government with a view to minimising the commercial damage that in a maritime city would be attendant upon the epidemic diagnosis of a disease capable of spreading to the shipping. In fact, seventeen years after, Palloni, in giving his advice on yellow fever to the sanitary authorities of the port of Marseille, confessed openly that there had been at Leghorn in 1804 an epidemic of yellow fever.

1883. The small epidemic at Torre Annunziata alleged to have been yellow fever occurred in 1883 on the eve of the devastating prevalence of Asiatic cholera at Naples the following year. The interest it probably would have otherwise attracted was lost in the greater epidemic that entirely occupied the activity and study of Italian physicians and epidemiologists.

The first case occurred June 19 in the person of a tavern keeper, aged 60, from Ischia. This man went directly from Ischia to Torre Annunziata, May 29, to transact business as a wine merchant. His case was

diagnosed as one of grave icterus and he died July 8, in Via Cisterna. A few days later another man, 80 years old, living in the Via del Popolo, two or three blocks away, died with the same symptoms. The attending physicians made a diagnosis of acute yellow atrophy of the liver. The third case was that of a woman aged 70 years who died August 25, after an illness of eight days. She lived in Via Garibaldi, within two blocks of the first cases. The same diagnosis of acute yellow atrophy was made.

Early in September, several persons living in Via Cisterna were taken sick about the same time and with the same symptoms. An alarm arose and strict sanitary measures were employed. September 6, a custom-house clerk in Via Cisterna was taken ill. He had a chill, pains in the back, high fever, slow pulse, severe headache, and black vomit. He died in 7 days. Cases continued to appear in the same neighborhood until October 13. There were in all 13 cases and 7 deaths. In September, a commission of medical men from the University of Naples investigated the disease. Among them was Professor Somma, who died in the cholera epidemic at Naples the next year. After much discussion the members of the commission admitted the specific nature of the malady, but did not give it a name. However, Professor Somma, in a concise letter written September 24, 1883, to Dr. Gennaro Cozzolino, made the statement that the disease prevailing at Torre Annunziata was yellow fever. During the height of the epidemic the most careful investigations were made; necropsies were conducted by the most skillful pathologists of Naples; a special lazaretto was established, and the most stringent measures of isolation and disinfection insisted upon. The disputes between medical men were numerous and more or less violent. As a result, the consensus of opinion excluded yellow fever. Icteroid typhus and infective fever characterized by jaundice were the diagnoses settled upon by the different physicians who went so far as to give it a name.

Since 1883. It is a frequent occurrence in Italian ports up to the present time to have vessels arrive from South American ports with a history of yellow fever on board during the voyage. But no cases of yellow fever on shore have been registered since 1883. Vessels with suspicious histories of the nature mentioned are invariably sent for disinfection to the Italian national lazaretto on the island of Asinara.

YELLOW FEVER IN GREAT BRITAIN.

1817. The brig *Britannia*, from Liverpool, after being in the port of Falmouth for six weeks, began to discharge a cargo of bales of cotton. No sooner had the unloading begun than yellow fever developed, but the disease was limited to the crew of the vessel.

1852. In the month of November, the steamship *La Plata* arrived at Southampton from Saint Thomas. Yellow fever developed aboard

while she was in the port of Southampton, and of the 14 seamen who were taken ill 7 died.

1857. The steamship *Tamar*, which was suspected of being responsible for the grave epidemic of yellow fever at Lisbon, Portugal, in 1857, entered Southampton shortly afterwards. She had had deaths on the passage from Spain and gave rise to several cases of yellow fever at Southampton.

1864. In this year there were a few cases of yellow fever aboard a vessel lying in the harbor.

1865. In the month of September a sailing vessel arrived at Swansea from Santiago de Cuba. Yellow fever broke out aboard while she was in port and 15 persons died. There were no cases reported ashore.

YELLOW FEVER IN AUSTRIA.

1894. The history of yellow fever in Europe concludes with 2 deaths from the disease in hospital in Trieste. The Italian steamship *Colombo* returned to Genoa from Brazil, having had yellow fever aboard. She was detained for disinfection. Two of her crew went by land to Trieste, where they were stricken with yellow fever and died in hospital. There is no record of an extension of the disease.

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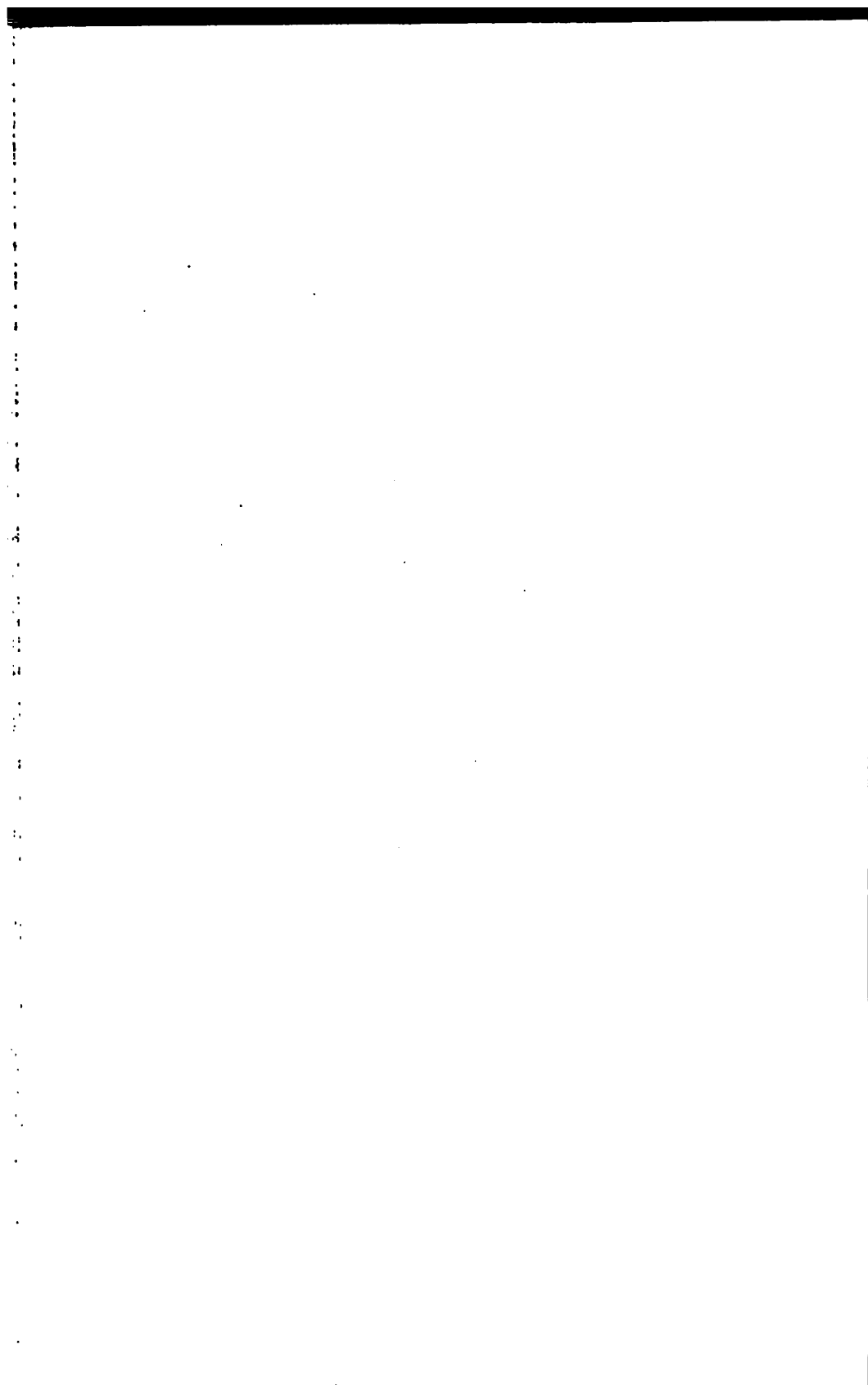
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YELLOW FEVER INSTITUTE, BULLETIN No. 9.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

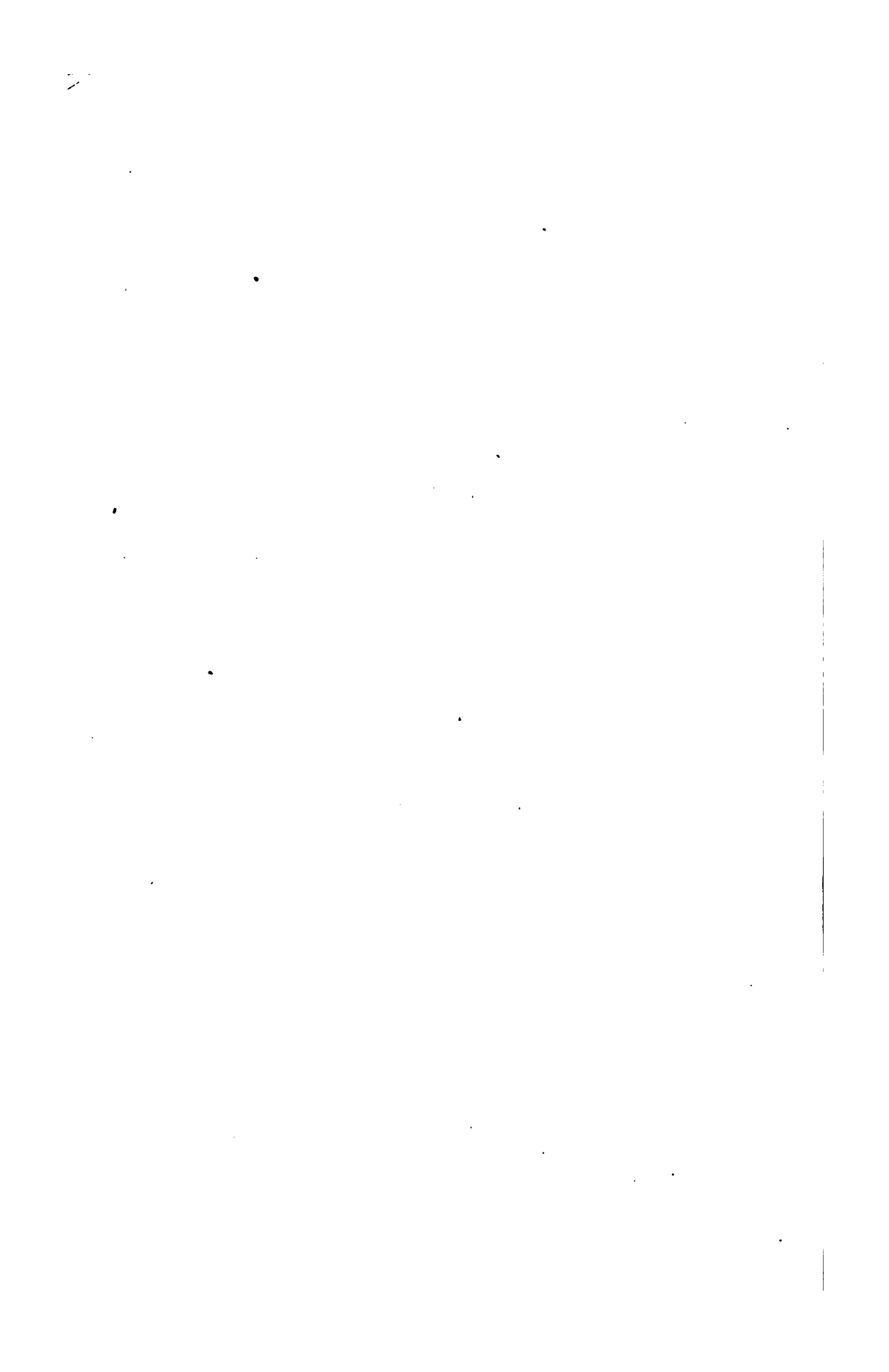
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Section C.—TRANSMISSION.

J. H. WHITE, Asst. Surg. General, Chairman of Section.

ARE VESSELS INFECTED WITH YELLOW FEVER?—SOME PERSONAL OBSERVATIONS.

By Surgeon H. R. CARTER.

JULY, 1902.

In a paper read before the American Public Health Association at Buffalo, September 18, 1901, Dr. Doty, the quarantine officer of New York, affirms the absence of secondary cases of yellow fever aboard vessels—i. e., that while cases of this disease contracted ashore develop aboard vessels, yet none are contracted aboard the vessel itself—that is, the vessel does not become “infected” with yellow fever.

The experience of other quarantine officers has been different, and it may be of service then to group some cases already of record in which the contrary was observed. It is not proposed to collate a number of examples of vessels aboard which yellow fever was contracted, from the literature of the subject, but to give very briefly the history of some such vessels personally observed by the writer, from his own notes, during a four years' service (1888 to 1891, inclusive) at the quarantine of the Gulf, Chandeleur and Ship islands. Here were received all vessels believed to be infected with yellow fever bound for all of the Gulf ports, except for New Orleans and from Tampa south. Consequently our clientele was considerable. The bulk of them, however, although certainly the worst class of vessels which entered the Gulf of Mexico, were not, in my opinion, “infected” when I received them—i. e., yellow fever could not then have been contracted aboard them.

I will premise here that I accept without reservation the conveyance of yellow fever by an infected mosquito of a certain kind, and that to

me a vessel "infected" with yellow fever is simply one which is harboring these infected mosquitoes. Whether they came aboard already infected or, being aboard, became infected by feeding on cases of yellow fever developing aboard ship but contracted ashore, can in general be determined from the history of the spread of the infection. Indeed, it was primarily the history of these and other ships which led to the (tentative) formulating of the laws of the "interval between the infecting and secondary" cases of yellow fever and the "period of extrinsic incubation of places" of that disease, which, and much else, are so clearly explained by the conveyance by a mosquito host.

The deductions as to the disease being contracted aboard the vessels, when such deduction is made, are, however, independent of the assumption of any theory of conveyance. I do assume, however, that the period of incubation of yellow fever, rarely, if ever, exceeds six or six and one-half days.

1888.—SHIP ISLAND.

I. Norwegian bark *Magnolia*, 946 tons, fifty-six days from Rio de Janeiro via Pensacola Bar, rock ballast. Left Rio de Janeiro May 20; left 2 men sick in hospital and had 1 aboard, considered yellow fever. Master sick third day out, May 22; died, May 27. All well till June 1, then several (3) got sick at once. First mate sick, June 11; died, June 17; black vomit. All were sick on the way up except 2; 21 on crew list including the 2 men left in Rio de Janeiro. One of these who escaped fever had had yellow fever, and the other was a lad from Dantzic on his first deep-sea voyage. In all 17 men were sick of fever en route, of whom 5 died. The last case, Elias Eliassen, developed June 14. Here, save the captain, all sickened not less than eleven days after leaving Rio de Janeiro, and the first mate and Eliassen on the twenty-third and twenty-sixth day, respectively. They then contracted yellow fever aboard ship.

The picture is that of an infection introduced aboard the vessel by the men who sickened in Rio de Janeiro—i. e., there were uninfected *stegomyia* aboard which were infected from these cases and conveyed yellow fever to the remainder of the crew, except the captain, who contracted it ashore. I did not record the dates of the cases of the men left at Rio de Janeiro; it was shortly before clearing. The interval between an infecting and a secondary case is almost always fourteen days or over.

II. Italian bark *Riagino*, Rio de Janeiro, for Pensacola, fifty-one days out; rock ballast, 560 tons. No sickness in Rio de Janeiro until just before leaving, then sent 2 men to hospital. Left five days after. Log shows men were taken June 4 and June 6 and removed on June 6. Sailed on June 10. No one had been ashore save master and steward, using a harbor boat.

First case reported sick en route June 21; 1 next day; 6 sick en route;

3 deaths, June 28, June 29, and July 14, all with black vomit. Crew refused duty at second death. Last case well July 13. Sixteen on crew list; 2 in Rio de Janeiro. Master had had yellow fever; steward sick just after leaving, not considered yellow fever.

Six cases developed ten days after leaving Rio de Janeiro. Same remarks as were made of the *Magnolia* apply here.

No record is made of where these 2 vessels lay in Rio de Janeiro, the writer not then appreciating the importance of this.

1889.

My notes for 1889 are lost, and indeed there may have been in 1888 more than the 2 vessels given above, which should have been included in this paper; but my notes, taken at first solely with the view of determining the period of incubation of yellow fever, give data on only these two sufficiently definite to determine that they were infected—i. e., that yellow fever was contracted aboard.

1890.

III. British ship *Avon*, in rock ballast; 22 in crew, 4 immune to yellow fever. Sailed from Rio de Janeiro April 20. All well in port and en route until thirty-eight days out, when a boy in port watch sickened with yellow fever. Taken to hospital, Gulf Quarantine, on third day, and died on sixth day. Another case developed two weeks later in a quarantine attendant who helped me clean up the room, sail locker, in which the boy was sick aboard ship.

It is remarkable that there should have been only 1 case of yellow fever among the crew aboard this vessel. At the time it was ascribed to the fact that this boy, the only one on the port watch, helped a man, shipped in Rio de Janeiro and immune to yellow fever, overhaul his chest a few days before the boy was taken sick. Whether there was an infected mosquito in the chest which had survived this length of time, or whether there was any relation between the chest and the fever, may be a question. It in no wise affects the present question, that the disease was contracted aboard. It was the first case seen at this station that year.

IV. British ship *Curlew*, from Rio de Janeiro, with rock ballast. No sickness was reported en route, in port, or on arrival. She was cleaned July 22 to July 23, 1890, and disinfection completed July 25, in the afternoon. One case of yellow fever developed July 27, the sixty-fourth day out, in the early morning before day.

V. British ship *Chippewa*, from Rio de Janeiro, with rock ballast. No sickness was reported in port, en route, or on arrival. She was cleaned July 26 and July 27, and disinfection completed July 28. One man, the quartermaster, developed yellow fever July 29, at night, sixty-eight days out from Rio de Janeiro.

The *Avon* made no port after leaving Rio de Janeiro and communicated with no vessel en route. The other 2 made no port save Pensacola Bar, and communicated with no vessel save the pilot boats there and off Mobile Bar. The infection in these 3 vessels, then, must have been contracted aboard. They lay in open roadstead at my station, 1½ miles off shore and about ½ mile apart, and there was no visiting between them and none of their crews was ashore.

VI. Spanish bark *Castilla*, fifteen days from Cienfuegos via Round Island Quarantine, in rock and earth ballast; 14 in crew. Eight days out from Cienfuegos to Round Island. All well in port, en route, and on arrival. Mate sickened fourth day after arrival at Round Island while discharging ballast. Vessel sent here in tow August 22. Mate had yellow fever; died on the sixth day of illness. Captain developed yellow fever day after mate's death; taken to hospital. No other cases of sickness aboard; the remainder of the crew are, save 1, Manila men, and all probably immune to yellow fever, being mainly residents of Cuba for many years.

Here 2 men developed yellow fever, 1 twelve and 1 seventeen days after leaving Cienfuegos. The infecting mosquitoes may well have been harbored in the hold, which the mate would probably not have visited until he anchored at Round Island and began discharging ballast, and in which the master would not be apt to go while the mate was on duty.

VII. Spanish bark *Grand Canaries*, seven days out from Havana July 7. All well in port, en route, and on arrival and while in quarantine. Crew probably all immune to yellow fever, being mainly Manila men and old residents of Havana.

O. F., quarantine employe, went aboard as ballast master; next day developed yellow fever, July 11. This man had been exposed to no possible source of infection for the six months previous except this vessel. A case nearly similar to the above occurred in 1889, but I have no notes of it.

VIII. Norwegian bark *Queen of the Seas*, in rock ballast, Rio de Janeiro for Pensacola, fifty-four days out. Left Rio de Janeiro with 17 men; 6 deaths en route. All well in Rio de Janeiro. Lay at Mocanque, a healthful part of harbor. None save master allowed ashore, but he went in ship's boat. Left 1 man at Rio de Janeiro—consumption. Shipped 1 man, a negro, in his place. Sailed April 23; master sick April 26; second mate sick night of May 10; 2 men May 11; 1 man May 12; 2 men morning of 13th; 2 during day of 13th; 1 man sick and 1 died 15th; 1 man died 17th; 2 sick 17th; 1 died 19th; 2 died 21st and 22d; 1 sick 21st; 1 died 25th; 13 sick en route, 5 died. The man shipped in Rio de Janeiro (negro) and 1 of the others immune by previous attack. The picture is very clear of a clean ship, infected by the illness of the master contracted ashore—i. e., had uninfected mosquitoes aboard, which became infected from the master sick of yellow fever, and conveyed it to the crew.

1891.

IX. British ship *Ourlew*, fifty-seven days from Rio de Janeiro for Pensacola. Lay in the Gamboa last eight days. Two men sick February 27, taken to hospital that day; sailed March 1. Master sick March 1; 5 men besides him that night. Two men March 4, 1 March 5, and 2 more during the day. Two men sick March 7. Two men died the 19th, sickening the 13th and 15th, respectively, both with black vomit. All aboard here, 19, were sick en route except 1, a Barbados negro; but don't believe all had yellow fever, the crew having been badly frightened. The earlier cases and the 3 who died were undoubtedly yellow fever, as were the steward and mate. Here we have 2 cases, at least, developing thirteen and fifteen days after leaving Rio de Janeiro.

X. Swedish ship *Condoren*, seventy-nine days out from Rio de Janeiro via Pernambuco for Mobile. Rock and earth ballast; 18 in crew. All well in port. Lay in Gamboa last five days. No shore leave allowed, but took ship's boat to go ashore. Sailed March 3; 3 men sick March 5; 16 men sick, all told, up to March 26, and 6 deaths. Last man got sick March 26, when she put into Pernambuco short-handed and sent 3 sick men to hospital. Two men sick March 20; 4 men sick March 18; 1 man sick March 26 (really night of 25th). At Pernambuco she lay eleven days and was disinfected by sulphur. Shipped 8 new men, 4, probably 5, of them immune to yellow fever. Developed no sickness on the rest of the way up. Here 4 men developed yellow fever fifteen days from Rio de Janeiro.

XI. German ship *Gustav and Oscar*, Rio de Janeiro for Pensacola. Lay at Cobras, a healthful place. One case yellow fever at Rio de Janeiro, March 22, sent to hospital March 24. No shore leave allowed. Sailed from Rio de Janeiro April 1; first case sickness April 7, 2 men; 3 next day; 1 next morning, and 2 during the day of the 9th. One death on the 10th, leaving 6 men sick. Captain sick on the 10th at night after supper. Last case on 14th. Two deaths on 11th; 1 on 12th. Crew list shows 21 men left Rio de Janeiro; 14 sick and 4 deaths en route. It is reasonably certain that 4 of the remaining crew were immune to yellow fever by previous attack.

XII. Norwegian bark *Crown Prince*, fifty-eight days out from Rio de Janeiro for Ship Island. Lay at Moncanque. No sickness aboard in Rio de Janeiro. No shore leave granted, and did not use ship's boat to go ashore. Sailed April 29. Master sick second day out (April 30). Next case May 16; 3 (2 aft and 1 forward) became sick. May 17, 2 sick in morning, 1 in the day. May 18, 3 men in fore-castle sick. May 20, 2 sick, 1 death. May 21, 1 death, 1 sick. May 23, 2 deaths. May 24, 1 sick. May 28, 1 death last night. May 29, 1 sick this morning. M 0, 1 death. The 1 case on the 29th was the last case taken sick. There were 14 men aboard and every man had fever, 6 dying. She put into Barbados on June 10, disinfected and shipped (in quarantine) 4

new men, 1 probably unacclimated. No more sickness en route. All of these cases except the captain's were not less than sixteen days from Rio de Janiero before developing.

XIII. French ship *Emily Postel*, twelve days from Vera Cruz via Pensacola quarantining. Had "sickness" aboard just before leaving Vera Cruz, 1 man. Sailed from Vera Cruz July 28; no sickness since until crew went to discharge ballast, August 12. One man sick yellow fever August 15, 2 men the same, August 19, and 1 man August 20. Disinfection by sulphur was done on the appearance of the first case of yellow fever and no case occurred save the above. All were developed more than sixteen days after leaving Vera Cruz, hence from infection on board. The history points to infection (infected mosquitoes) in the hold.

The picture given by the *Ourlew* and *Conderen* are those of disease conveyed by mosquitoes coming aboard already infected just before they sailed. The infection was not introduced by the men who first sickened, the interval between them and the next cases was too short. Observe that they lay in the Gamboa, directly in the lee of a town badly infected. The other two give the usual history of a clean place (town or vessel) infected by some one developing yellow fever, contracted elsewhere, in it.

XIV. Dr. G., assistant surgeon U. S. Marine-Hospital Service, developed yellow fever June 18 at the Gulf Quarantine Station, and died June 29. He was immediately from New York, where he had been on duty some months, and had been at the station but fourteen days when he was taken ill. There had been no case of yellow fever at the station that year. There were a number of vessels in quarantine, but the *Gustav* and *Oscar* (No. XI) was the only one I judged to be infected. On this vessel, as on the others, he had been with me inspecting, opening up drawers and boxes, and going into every compartment, etc., for the disinfection. I thought his infection was from this vessel. It was certainly from some vessel.

I think it will be granted from the above that the ability of a vessel to carry the infection of yellow fever is no myth. Here are 13 vessels which did so carry it collated from only three years' observation at a single station. Such vessels are indeed rarer, much rarer, now than they were before 1894, yet they still come. I saw 2 at Tortugas in 1894. Other cases are reported by Geddings and by Echemendia at the same place and at Port Tampa quarantine. Rosenau reports a case contracted aboard the steamship *Vigilancia*, from New York, plying between New York and Vera Cruz via Havana, in 1899. The steamship *Bodo*, last year (1900), from Bocas del Toro, for Mobile, developed 3 cases of yellow fever, seven, eight, and nine days out from Bocas del Toro. It would not be difficult, I think, to multiply instances of recent date, yet that they are rarer is without question. On the factors which have brought this about we can barely touch.

Obviously there are two methods by which vessels can become infected. (a) A case of yellow fever contracted elsewhere may develop aboard a vessel already harboring *stegomyia* mosquitoes which become contaminated from it. (b) The *stegomyia* mosquitoes may come aboard already contaminated. In the first case, there being nearly always over two weeks between the infecting and the first secondary cases of yellow fever, it results that, if the first case occurs after leaving port, vessels, even sailing vessels, from Cuba and the Caribbean Sea will generally reach quarantine and (if at a southern station) be disinfected—i. e., mosquitoes killed, before it is time for the secondary cases to develop, or, indeed, to be contracted. This agrees with all observation. In vessels infected in the second way, cases of yellow fever may occur after a very short or no interval from leaving port. The causes, then, which have lessened the number of infected vessels at United States ports, are—

1. The very great falling off of vessels from Rio de Janeiro and Santos since the establishment of the Brazilian Republic. This does away with the bulk of the "long-trip vessels" we used to have, which are the only ones developing secondary cases en route if infected by a case of yellow fever developing aboard. (Vide a.)

2. The replacing of sailing craft by steamships. That steamers convey yellow fever less frequently than sailing vessels has long been known. This is because they lie a much less time in an infected port, and the discipline of their crews is better; no shore leave means no man goes ashore. They also make quicker trips, and thus are not apt to develop secondary cases en route, even if yellow fever contracted elsewhere develops aboard and they have the *stegomyia* aboard. It is also to be noted that the worst parts of the harbors of Havana and Rio de Janeiro, above San Jose wharf and the Gamboa, have never been berths for steamships. Note, too, that the sailing vessels displaced are the foreign sailing vessels; the American schooner was less often infected than foreign vessels.

3. Especially since 1893, and to some extent before supervision had been kept by United States sanitary inspectors in the more dangerous yellow-fever ports over vessels bound for the United States, especially of passenger vessels. Certain anchorages have been recommended as safe, others have been forbidden, notably the Gamboa at Rio de Janeiro and certain wharves and parts of the harbor at Havana. Passengers who it is believed will develop infection aboard have been barred; shipment of new men in the infected port carefully supervised; vessels in which yellow fever has occurred in port are disinfected before leaving, and many other measures taken to have the vessel leave port clean, or as nearly clean as commercial considerations allow. In general, the vessel owners, especially of the regular lines, have given hearty cooperation in these measures, as well as in keeping the crew aboard and in confining the visits of such officers as must go ashore to daylight.

These restrictions, especially the last, have by no means been absolute for all classes of vessels, but are well observed, in Cuban and Mexican ports at least, by probably over five-sixths of the tonnage. The sanitary measures to avoid infection (3) and the proportionate substitution of foreign sailing vessels by steamships (2) are without doubt the main factors acting in cooperation in lessening the infection of ships. No one can read Burgess' list of infected vessels in Havana Harbor (Report, U. S. Marine-Hospital Service, 1896) without noting how great has been that decrease in recent years.

We have said that if a case of yellow fever develops aboard a vessel harboring the *stegomyia* mosquito (proper conditions of temperature being premised) that they may become contaminated by feeding on him and infect others. A vessel which has no *stegomyia* aboard is like "noninfectible territory" and will not communicate infection, even if cases of yellow fever develop aboard. I think it fair to say that vessels plying to and from southern ports of the United States will, during the summer season, generally have the *stegomyia* aboard, independently of its berth in tropical harbors, and may at times breed them in their water supply. This mosquito, however, seems to be rare north of Virginia Beach (its distribution has not been sufficiently investigated, however), and a vessel plying to and from a northern port of the United States would not harbor this mosquito unless it came aboard in the tropical port. Now how far this mosquito goes or is borne from shore has not, I think, been directly investigated, but we do know that the crews of vessels moored off from shore (say 200 or more fathoms) in that part of Havana harbor seaward from the line between the Sta. Catalina warehouses and the Machina wharf do not develop yellow fever (unless close to some vessel which is infected). This means that contaminated *stegomyia*, at least, do not go so far from shore. Lying then at the anchorages accounted safe in Havana harbor, where the passenger vessels for the United States lie, one would think that the probability of any *stegomyia* coming aboard would be small. At Vera Cruz the vessels must lie nearer shore (although to windward of it), and experience shows that the crews of vessels lying there are not entirely safe, as I believe them to be in Havana, although infection in the part of the harbor picked out as safe is decidedly rare. The anchorages in both harbors regarded as safe are well to the windward of the town all summer. A direct investigation of this matter—i. e., the presence of the *stegomyia* aboard vessels from northern ports in different parts of the harbor of Havana and other tropical harbors, should be made.

To sum up—

1. Vessels aboard which yellow fever had been contracted—i. e., vessels infected with yellow fever have not been rare, at least at southern quarantine stations.

2. Such vessels are much rarer since 1893, and are not very common now.

3. That the diminution of the number of infected vessels reaching United States ports is due mainly to the sanitary measures for avoiding exposure to infection in the foreign port, and to the substitution of steam for sailing vessels. To some degree the falling off of the vessels from Brazilian ports is also a factor.

4. That a case of yellow fever developing aboard a vessel plying between southern ports of the United States and the tropics will probably infect the vessel so that other cases can, if time be given, be contracted aboard her.

5. Such vessels, however, if short-trip vessels, not more than ten or twelve days en route after the occurrence of the case of yellow fever, will in general be disinfected at southern quarantine stations before any other cases have been contracted aboard, although harboring infected mosquitoes.

6. That a case of yellow fever so occurring aboard a vessel from a northern port of the United States would be able to infect her or not according to whether she had acquired the mosquitoes *stegomyia fas.* in the tropical port.

7. It is, in general, then necessary to disinfect all vessels running between southern ports of the United States and tropical ports if a case of yellow fever occurs aboard, no matter where it be contracted; while vessels running between northern ports and the tropics may, through precautions in tropical harbors, have no *stegomyia* aboard and are thus not infectable by cases of yellow fever occurring aboard.

8. Some vessels giving no history of yellow fever in port, en route, or on arrival—even when many days en route—are nevertheless infected and communicate the yellow fever to those who go aboard, vide Nos. IV, V, VI, VII. Note, also, the first case aboard the *Avon*, No. III, was thirty-eight days out from Rio de Janeiro. This is probably due to the infection (infected mosquitoes) in parts of the vessels unfrequented by the crew while en route, or to the crew being all immune to yellow fever.



YELLOW FEVER INSTITUTE, BULLETIN No. 10.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

THE METHODS OF THE CONVEYANCE
OF
YELLOW FEVER INFECTION.

By Surgeon H. R. CARTER.

JULY, 1902.

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YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 10.

Section C.—TRANSMISSION.

Asst. Surg.-Gen. J. H. WHITE, Chairman.

THE METHODS OF CONVEYANCE OF YELLOW FEVER INFECTION.

By Surg. H. R. CARTER.

JULY, 1902.

Whether further experimentation is desirable before we accept without reserve the *Stegomyia fasciata* contaminated by a patient sick of yellow fever as the *only* natural means of conveying yellow fever may be a question, yet I think that the argument for its being in nature conveyed only by a host, and doubtless a mosquito host, is strong. It is assumed that there is no question that it may be thus conveyed.

1. Analogy: Of such diseases as have been fully investigated, all that are conveyed from living hosts are caused by animal parasites. Also of these diseases each one *is conveyed (in nature) only by means of a host of a given genus.*

2. Agreement of facts observed about the propagation of yellow fever as it occurs in nature with the necessary deductions from the theory of conveyance by this host.

(a) The fact that the disease is not directly propagated from the sick to the well, that it is propagated only by means of an infected environment.

(b) That a man sick of yellow fever may infect his environment.

(c) The existence of "infectible" and "noninfectible" territory. (a)

^a An "infectible" place is one which, if cases of yellow fever be introduced therein, becomes infected—i. e., capable of inducing yellow fever in those who, susceptible to that disease, visit or live there. A "noninfectible" place is one which will not become infected even if cases of yellow fever be introduced. In such a place yellow fever is not a transmissible disease. The theory of conveyance by a host would explain the difference by the presence of the proper host (*Stegomyia fasciata*) in the one and its absence in the other.

that baggage from Havana and Vera Cruz will not convey yellow fever directly to people after the voyage to New York or Spain, thus that yellow fever is not conveyed by mosquitoes carried in such baggage.

Whether this time element is necessary, of course, is not determined by these observations, but it is a factor in them.

Whether the rare cases of yellow fever we sometimes see contracted from infection aboard ship hitherto uninfected may be due to infected mosquitoes brought aboard in the hand baggage of passengers, and opened soon after coming aboard, may be a question. The sister who developed yellow fever aboard the *Vigilancia* en route from New York to Havana, is a case in point, and we occasionally see members of the crew with yellow fever. One occurred in Havana harbor on a Ward liner en route from Vera Cruz to New York in 1900. Other explanations of these cases may, of course, be possible.

With the above should have been considered in addition from 175,000 to 200,000 persons, troops, and families returned from Cuba by transport at the end of the war, with baggage and equipment. As to the positive instances of conveyance by baggage which have been reported, none that I have been able to inquire into personally, certainly exclude this method of conveyance. The reporter begins (as I did) with the assumption that yellow fever is conveyed by fomites, and as soon as he can show the introduction of fomites from an infected place, he is satisfied. He looks no further for any other source of infection. Strange to say, the *best* attested cases I have come across have not been those of conveyance by *packed* baggage, but by *clothing worn on the person*, sometimes for a number of miles, or hours through the sun and air, which is against all other experience of this disease. Of the older reported cases I have nothing to say; I can not examine them; only as none of the modern ones which I have been able to inquire into clearly exclude other means of conveyance, it is fair to at least doubt if the older reports are impeccable. Also it is common sense, that when there is a great mass of negative testimony on a subject, all tending one way, we may not accept a moderate amount of positive evidence in rebuttal unless its *data be conclusive*, and I think the evidence of the Cuban and Mexican baggage is great enough for this rule to apply. I think then we may reject the conveyance by fomites as not proven, and say that there is no good evidence in rebuttal of conveyance save by a host.

Now, let us look at this evidence. The argument from analogy, in this case has great weight. The presumption that it creates is strong.

For the second argument. It is indirect evidence, of course, yet it is the kind that we accept for the theories of the causation of other kinds of natural phenomena. That the deductions from the theory agree with the observations of the phenomena is the only evidence we have for the doctrine of universal gravitation, of the vibration of light, of the conservation of energy, etc., which physicists hold as beyond cavil. It is true we have been able to apply mathematics to these theories, and that the chain of phenomena which we can thus compare is much greater than we have in this instance; yet I think that we can fairly claim that in our case *all the phenomena which we have fully*

examined agree with the deductions from the theory and none disagree, and the *principle* of deciding on *the truth of the theory is the same*. I think then that the evidence (presumptive only) is good, that the only means of conveying yellow fever is by means of a mosquito host.

This evidence is indirect and presumptive only. Yet it seems easy to obtain *some* direct, although negative, evidence—i. e., to show that other methods (besides the host) do *not* convey infection. Could we show that *no* other methods *ever* convey infection it would be a demonstration.

To look at the matter broadly, there are usually three *atria* of entrance of an infection: (1) By the alimentary canal; (2) respiratory tract, and (3) abraided or punctured integument. For yellow fever the first is not accused. The negative evidence against conveyance by drinking water is overwhelming, and while that against foods is less so, still it is great, and there is no evidence whatever *for* it so far as I know, and no one claims it.

To exclude the second one. If we could place a certain number of people in an environment infected with yellow fever—i. e., an environment in which cases of yellow fever *were being contracted* (not simply where such cases existed), living in all respects like those who are contracting the disease, but protected against mosquitoes, and these people should fail to contract the fever, it would be evidence that the single factor present in the case of those contracting the fever, but absent in their own—i. e., the mosquitoes puncturing the skins of one set and not of the other, was the cause of the different results in two sets of people. I say "evidence," and this evidence would be convincing in proportion to (1) the degree of infection of the premises as shown by the proportion of those entering them who contracted the disease and (2) the number of susceptible people exposed and the length of their exposure. It is somewhat strengthened if these same people who escape afterward develop fever from mosquito inoculation; but this is not necessary if enough people are subjected to the experiment. Such evidence would never, strictly speaking, be proof; yet could such an experiment be made in a house like the Grey House, at Orwood, in 1898, where of 32 people who entered the house, some only to stay a few hours, 31 developed yellow fever *from that exposure*, the exposure of a very moderate number of people, not immune to yellow fever, thus isolated from mosquitoes, would be convincing to me. I can conceive of no other test which will *directly* show that conveyance of yellow fever does not take place by the respiratory tract.

We have seen that the theory of conveyance by a host explains all the facts which we know of the conveyance of yellow fever. Does any other theory also explain them? If so, it also has a right to be considered.

It is proven that yellow fever is not in nature transmitted directly from the sick to the well. It is propagated from the sick man by his

infecting his environment, from which only is it contracted by others exposed thereto. This is nowise in accord with the methods of conveyance of known bacterial diseases, all of which are conveyed by material directly from the patient inhaled or injected by, or (as with leprosy) applied to an abraded surface of, the one who receives the infection.

From this it is a *necessary* deduction that the disease is not in nature propagated by material conveyed directly from the sick to the well; that some material after leaving the body of the patient *undergoes some change* outside of his body, and *after* this change produces yellow fever in one susceptible to that disease.

This change, which takes place outside of the body of the sick man, may be:

A. A change in physical condition of the excretion containing the microorganism rendering it able to reach the proper atrium for the infection of others. Analogous to the drying and pulverization of tubercular sputum, etc.

B. The infection of a host, by which host (or its offspring) the microorganism is transmitted analogous to the transmission of malarial fever or the Texas fever of cattle. This may involve no change in the organism itself. It may simply place the organism in a position to enter the human organism by the necessary atrium, as directly into the circulation or lymph spaces. Of course it does not *negate* such change.

C. A change in the microorganism itself, it undergoing development outside of the human body into some stage different from that in which it leaves the body. This last has been the theory accepted by most of the writers who have considered this subject, but there is no analogy with the propagation of any other disease, so far as is known to the writer.

No other hypothesis is to me conceivable.

Also it is proven that not all environments become infected—i. e., capable of inducing yellow fever in those exposed in them by the presence of people sick of yellow fever; that there are places which become, habitually become, infected if cases of yellow fever be introduced at certain seasons of the year and others which do not and into which the introduction of such cases causes no infection of the environment.

Certain conditions of the environment, then, even in the presence of the yellow-fever patient, are necessary for it to become infected. Besides temperature, moisture, and altitude, there are others of which we are ignorant, and many localities habitually have not received infection from the presence of the sick, although there are no differences in soil or climate, which we could appreciate, between these localities and others that did so become infected.

This quality of a place, its being infectible by yellow fever, sometimes, probably frequently, varies from year to year. Cases of yellow fever may be introduced some summers with impunity, and in others in

the same place spread on introduction. Compare the results at Ferandina in 1876 and 1877.

Now, of the three hypotheses, A, B, and C, the first is, I think, not compatible with what is known of the infectibility of places, and which is so well known that we have only alluded to it above. It is not reasonable that the conditions which determine the physical condition of the infective material should be those that we know to influence the infectibility of places, or that they should be so elusive to meteorological tests as the latter have proven.

The third is negatived by the proven fact (Reed and Carroll) that the blood or serum of a yellow-fever patient injected hypodermatically into a well man will produce the disease in him. The microorganism then exists in the blood of the patient, and consequently in the bloody material extruded from him (gums, etc.) in a form capable of producing the disease. No change of development is necessary if it can only be introduced into the circulation directly.

The second hypothesis of the three, which alone seemed admissible, is then the only one not incompatible with the facts which we know of the propagation of yellow fever, and we have seen previously that it is *entirely compatible* with them.

To sum up :

For the belief that yellow fever is conveyed in nature *only* by a host and doubtless a mosquito host, we have—

1. The analogy of other diseases conveyed by insect hosts.
2. That all facts observed about the propagation of yellow fever agree with the necessary deductions of this theory.
3. No other theory explains all the facts observed of its propagation.

The second postulate, may be, I think should be tested further by the collection of other facts to be compared with the theory; possibly on the lines given above, for obtaining direct negative evidence about this theory of conveyance. Yet the evidence already extant seems to the writer convincing and he is convinced that yellow fever is conveyed in nature *only* by a mosquito host of a particular kind or kinds.

YELLOW FEVER INSTITUTE, BULLETIN No. 11.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

**VESSELS AS CARRIERS OF
MOSQUITOES,**

BY

Passed Asst. Surg. S. B. GRUBBS.

MARCH, 1903.

**WASHINGTON:
GOVERNMENT PRINTING OFFICE.
1903.**

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YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 11.

Section C.—TRANSMISSION.

Asst. Surg. Gen. J. H. WHITE, Chairman of Section.

VESSELS AS CARRIERS OF MOSQUITOES.

By S. B. GRUBBS,

Passed Assistant Surgeon, United States Public Health and Marine-Hospital Service.

At the present time, when evidence is pointing with more and more clearness to the mosquito as the sole means of transmitting yellow fever, nothing is of greater interest to the quarantine officer than to decide to what extent and under what circumstances these infecting insects may be carried by vessels.

This subject may be approached in three different ways: First, by observations on the length of time after leaving infected ports vessels may develop yellow fever; second, by experiments with mosquitoes under artificial conditions made to simulate as much as possible those of nature; and third, by actual observation of vessels arriving from ports at the time infected or where the presence of the *Stegomyia fasciata* render them liable to infection.

While it will require data obtained by all these means and extending over a long period to arrive at any conclusions sufficiently accurate to allow them to influence quarantine procedure, still I believe the last method of observation cited will throw more light on the subject than the first two.

It is for this reason that every vessel arriving at Gulf Quarantine Station from *Stegomyia*-infected ports has, since the 1st of July last, been carefully examined to ascertain if mosquitoes were present on board, and, if present, their variety, where and when they came aboard, and under what conditions.

Gulf Quarantine Station is an especially good point for these observations, from the fact that it is 10 miles from the mainland, and because vessels bound here do not pass near land, and so but rarely take on mosquitoes en route, and even these, as will be seen, are

always the marsh-bred varieties of *Culex*. Besides, the examination of at least a thousand mosquitoes on Ship Island has convinced me that there are no *Stegomyia* here.

Each vessel inspected was carefully searched, the inspector being armed with a cyanide killing bottle, and in addition the captain was asked the following questions:

1. Were there any mosquitoes on board on your outward voyage, consisting of — days?

2. If so, did they come aboard before departure from home port or at sea, and under what circumstances?

3. Were there any mosquitoes on board at your destination or on homeward voyage?

4. If in port—

(a) How far were you from shore?

(b) Prevailing wind and weather?

5. If on homeward voyage (consisting of — days)—

(a) Were they from port?

(b) Did they come aboard at sea, on what day, and how far were you from land?

(c) Were there wigglers in any of your tanks at any time?

During the five months from June 1 to November 1 observations were made on 82 vessels, all arriving from ports where the *Stegomyia* is believed to exist in quantities. Of these 78 were sailing vessels and 4 were steamers.

Of these 82 vessels 65 claimed to have had no mosquitoes aboard at any time during the voyage or at port of departure, and their absence having been confirmed by search, we can dismiss them from consideration and pass to the remaining 17.

Five of these had mosquitoes on board at their ports of departure, 2 being rid of them as soon as they were well at sea, while 3 others carried them two days and were then no more troubled, except one schooner on which they reappeared in quantities five days before she reached this port, when she was 20 miles from shore.

Nine sailing vessels, having no mosquitoes on board before sailing, had them appear at sea, in one case from the water casks in which the captain found larvæ. But in the other cases they doubtless came from land which was at the time distant—20 miles in one case, 15 miles in three cases, 10 miles in one case, and 2 miles in the last two instances. In all these vessels the mosquitoes found on board on arrival at this station were the common varieties of *Culex*, there being no *Anopheles* or *Stegomyia* among them.

Stegomyia fasciata were found on board and were identified in the remaining three cases, as follows:

The schooner *Susie B. Dantzer* arrived from Vera Cruz, Mexico, on July 16, 1902, after a voyage of fifteen days. The captain stated

that mosquitoes came aboard in large quantities at Vera Cruz, although he lay a half mile from shore and there were variable winds with squalls and rain all the time. The number of the insects decreased on the voyage but were always in evidence, and we caught four or five of them here. No larvæ were found in any of the tanks, and as the captain had repeatedly examined them without result in his efforts to be rid of the mosquitoes, I believe the insects found on board here came all the way from Vera Cruz.

The schooner *Eleanor* arrived from Vera Cruz on July 17, 1902, thirteen days out. She had no mosquitoes on board before reaching Vera Cruz, but there quantities came on board. Her moorings were half a mile from shore and the winds were variable. The captain stated that he could not get rid of the insects after sailing, although the number decreased very much and there were no larvæ in any of the tanks. At the time of her inspection here we caught and identified a number of *Stegomyia*.

The brigantine *John H. Crandon* arrived at the station July 27, 1902, twenty-two days from Vera Cruz, where she had one case of yellow fever on board. At that port she lay a half mile from the sea wall, three-eighths of a mile from an infected prison, and within 200 yards of an infected vessel. *Stegomyia fasciata* were found on board by Acting Assistant Surgeon Hodgson before she sailed, as well as larvæ in the tanks. All during the trip there were mosquitoes in abundance, and a veritable plague of *Stegomyia* was found on board on her arrival here. There was a constant buzz in the forecastle, and anyone entering was sure to be attacked by several mosquitoes. Specimens were caught in almost every protected part of the vessel, and all were found to be the *Stegomyia fasciata*. The captain had emptied several water barrels because he found they were breeding mosquitoes, but the water remaining had no live larvæ, although many old moults were seen. As breeding was surely going on in the tanks during a part of the voyage at least, it would be impossible to say how long any particular mosquito had been aboard or if any of them had been brought here from the infected port.

SUMMARY.

The above facts may be summed up as follows:

Vessels having no mosquitoes on board at any time	65
Vessels having mosquitoes on board in port of departure	5
Vessels on which mosquitoes (<i>Culex</i>) appeared en route	9
Vessels arriving with <i>Stegomyia fasciata</i> on board	3

Three and a half per cent, then, of all vessels brought *Stegomyia* on a voyage averaging seventeen days.

CONCLUSIONS.

From but one season's observations at a single quarantine station we can not assume to draw any hard and fast conclusions regarding the probability of *Stegomyia*, infected or not, being carried by vessels. Nevertheless, I think we may conclude, first, that mosquitoes can come aboard vessels under favorable conditions when the vessel is not over 15 miles from shore; second, that *Stegomyia* can be carried from Mexican or West Indian ports to those of our Gulf States; third, that they can board a vessel lying at anchor a half mile or less from shore, being conveyed by the open lighters used or flying aboard, and finally, that a vessel moored a short distance from land may become infected with yellow fever, our old beliefs to the contrary notwithstanding.

I wish to acknowledge the aid of Assistant Surgeons Burkhalter and Ebersole in collecting data and specimens.

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YELLOW FEVER INSTITUTE, BULLETIN No. 12.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

THE EARLY HISTORY OF QUARANTINE:

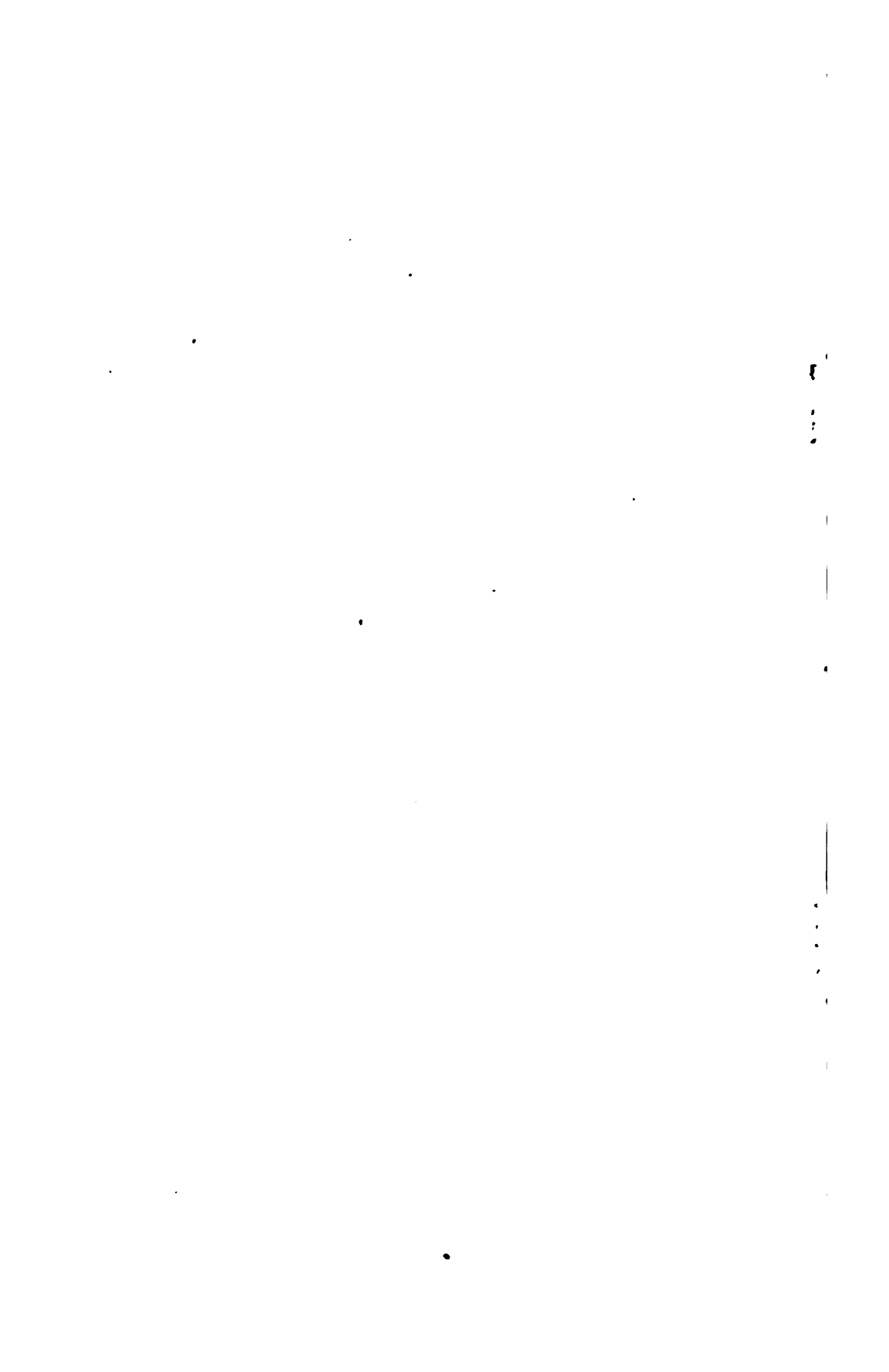
**ORIGIN OF SANITARY MEASURES DIRECTED AGAINST
YELLOW FEVER,**

BY

Passed Asst. Surg. J. M. EAGER.

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Section D.—QUARANTINE AND TREATMENT. Asst. Surg. Gen. W. J. PETTUS, Chairman of Section.

THE EARLY HISTORY OF QUARANTINE—ORIGIN OF SANITARY MEASURES DIRECTED AGAINST YELLOW FEVER.

By P. A. Surg. J. M. EAGER.

FEBRUARY, 1903.

The public sanitary measures included in the comprehensive term "quarantine" have been more extensively applied in America against yellow fever than against any other disease. Most of these measures had their origin long before yellow fever was known to the world. The way they came into existence and how they were later used as a protection against yellow fever is one of the most interesting topics in sanitary history—one without which no account of the prophylaxis of yellow fever would be complete. In the present writing the term "quarantine" is not limited to its narrower sense, but is taken to mean any restraint, owing to contagious disease, of intercourse on land or by sea. It includes such incidental measures as disinfection.

The history of quarantine is closely interwoven with that of medicine in general and of shipping. We read of these practices being applied against leprosy in biblical times, and Captain Cook, the English navigator, tells us that the savages of the South Sea Islands, who had not advanced beyond the stone age at the time of his visit to those islands, resorted to rude sanitary precautions in the case of arrivals from neighboring places.

The story of the beginnings of quarantine is associated particularly with the epidemiology of leprosy, pest, and syphilis. Cholera and yellow fever were later considerations. The first reported prevalence of yellow fever was at Bridgetown, Barbados, in 1647, the year before the great pest of Habana. At this time quarantine measures had been practiced against other malignant contagious diseases, a maritime quarantine station having been in operation at Venice in 1403, nearly a century before the discovery of America. It was only necessary to include yellow fever in the category of contagious exotic diseases and apply against the malady the procedures already in vogue. The first appearance of yellow fever in Europe occurred at Lisbon in 1723, and is described in the article "Yellow fever in Portugal" (Bulletin No. 4, Yellow Fever Institute, United States Public Health and Marine-Hospital Service). It was not, however, until 1821, following an extensive epidemic in Spain, that quarantine was applied in Europe against yellow fever. The Spanish academies were interpellated as to the nature of the disease, and as a result of their replies yellow fever was declared quarantinable. Inquiry in England in 1823 and 1824 was followed by an act of Parliament directing quarantine against yellow fever in the same way as against plague. Quarantine theory and practice have from the beginning followed medical dogma. Religion, astrology, and crude or false doctrines of etiology extended their influence. Like most branches of practical medicine, the practice of quarantine passed from the hands of priests into those of empiricists. It took ages for public sanitation to establish itself on a scientific basis.

LEPROSY AND LAND QUARANTINES.

The first quarantines of which any mention is made in literature were land quarantines used as a protection against leprosy. The ancients regarded this disease as of African origin, and Lucretius states positively that it first came from Egypt. In the Old Testament the first indications are found of precautions taken against contagious maladies. Leviticus, Numbers, and the First Book of Samuel give directions for the sequestration of lepers, first in the desert, then outside the camp, and afterwards without the walls of Jerusalem. In these books the inspection of persons for the detection of leprosy is detailed. Persons afflicted with skin diseases were directed to present themselves before the priests. An observation of each case was made, and, according to minutely described symptoms, isolation of the patients was ordered for a prescribed period.

The crusaders on their arrival outside the walls of Jerusalem found lazarettoes still in existence, and after taking the city from the Mussulmans sent all contagious maladies to these isolated places. The name Hospital of St. Lazarus was given to the place of sequestration. Returning to Europe, the members of the military expeditions brought

back with them not only numerous diseases, but also the word "lazaretto," as applied to a place for the isolation of the victims of communicable maladies. As a result lazarettoes were built outside the gates of nearly all the principal cities of Europe. Leprosy itself had, however, been introduced into Europe many centuries earlier. It is spoken of as a foreign disease by the earlier Greek and Latin writers. Pliny thinks that leprosy was introduced into Europe by Pompey returning to Rome from Syria after his celebrated triumph over fifteen nations in Asia. It is implied that leprosy walked with the three hundred princes before the triumphal car of the conqueror. These surmises give rise to the interesting query whether leprosy was not the first quarantinable disease introduced by sea. As a quarantinable disease leprosy takes precedence in several ways. For instance, it was the first quarantinable disease (quarantinable from the point of view of the United States quarantine regulations) of which the causative germ was discovered.

During the epoch of the crusades leprosy became widespread in Europe and resulted in the extensive establishment of isolation stations. Leper houses existed at Metz, Verdun, and Maestricht as early as the seventh century, for long before the crusades the disease had spread from Italy into the Roman colonies of Gaul, Britain, and Spain, and thence into the most remote countries. Mathew Paris estimates that at the time of the great epidemic of leprosy in western Europe succeeding the movement against the Mohammedans 19,000 lazarettoes were in operation in Europe. Religious orders conducted the houses bearing the name of St. Lazarus, but in northern Europe many dedicated to St. George were under secular supervision. Not only were persons suffering from leprosy and other contagious diseases sent to such asylums, but the insane and individuals whose separation from society was deemed an advantage to the populace or the ruling powers were also confined there. In these places of isolation quarantine measures, that afterwards had their application at maritime stations and ultimately were directed against yellow fever, developed primarily. Lepers were not strictly confined to the leper houses. They were, however, required to wear a special costume, to limit their walks to certain roads, to give warning of their approach by sounding a clapper, and to forbear communicating with healthy persons and drinking from or bathing in any running stream.

PEST AND EARLY VIEWS OF ETIOLOGY.

In connection with pest and later with syphilis the greatest advances of mediæval times took place in public sanitary methods, leading to the establishment of maritime and land quarantines. During the Middle Ages more attention was given to the isolation of leprosy than of other diseases now known to be virulently contagious, for the reason

that the minds of medical men were hampered by accepted doctrines. One of the first of these dogmas was founded on the fact that, while in the sacred Scriptures minute attention is given to precautions against leprosy and skin diseases, no measures are prescribed against pest. Yet most disastrous epidemics are recorded in the Old Testament.

By the word pest is understood not only bubonic plague, but the different epidemic diseases, whatever they may have been, that were formerly included under that term. In their application to this group of maladies the various doctrines of etiology had a most important bearing on etiology. The history is preserved in a great number of documents, many of them obscure and quaint, but all interesting as showing the gradual development of public sanitation. From an etiological standpoint the history of public hygiene in its relation to epidemiology is divided into four periods, during all of which widely diverse views of causation of epidemic disease were held, the state of knowledge in each successive epoch advancing nearer the truth. First came a chaotic period up to the time of Hippocrates, secondly the centuries that intervened from the time Hippocrates set forth his views of etiology to the middle of the sixteenth century, when Fracastoro, basing his observations on the epidemic prevalence of syphilis that extended throughout Europe, announced a theory of contagion. Then followed an interval lasting until the evidence of a living contagion gained credence. Lastly came the time when specific germs were found to be the cause of epidemic disease. The last era, however, brings the history of quarantine to such a recent time as to be outside the scope of the present writing.

The word plague as well as pest was given by ancient medical writers to any epidemic disease that wrought an extensive destruction of life. Oalen, for example, used the word in this sense. History is replete with epidemics. Instances of ancient prevalences are the disastrous disease, recorded in II Kings, causing the destruction of the Assyrian army; the plague of Athens, described by Thucydides; the great pestilence in the reign of Marcus Aurelius, that extended over almost the whole of Europe, and the plague of Justinian, descriptions of which are given by Procopius and Evagrius. The plague of Justinian lasted for fifty years and has a decided interest in connection with the present subject, having been introduced in all probability largely by sea. It began at Pelusium, in Egypt, 542 A. D. After spreading through Egypt it appeared the next year at Constantinople. In subsequent years it advanced over the entire Roman world, making its initial appearance in seaboard towns and radiating inland. Frequent epidemics occurred in succeeding centuries, one of the most important of which was the great cycle of epidemics in the fourteenth century, which has been given the name of the "black death." Throughout all

this extensive period notions and practices relating to public sanitation were being evolved in accordance with the prevalent tenets of causation. In the earliest period religion, superstition, and stellar influence took the principal place in the confused ideas of etiology. Ill-ordered doctrines led to all sorts of irrational practices. Among the Greeks, in the rites of Æsculapius, the sick were not permitted to enter the temples, where they underwent treatment, without first being purified by various baths, frictions, and fumigations. All this was accompanied by ceremonies similar to those practised within the temples, namely, magical performances and fervent prayers recited in a loud voice, often with musical accompaniment. As an accessory to the purification preliminary to being admitted, the patient was required to pass the night stretched on the skin of a sheep that had been offered as a sacrifice. Here he was ordered to compose his mind for sleep and await the arrival of the physician. Throughout these ages as well as in more recent times a fanciful association between the phenomena of the material world and the destinies of mankind closely linked the doctrine of etiology with astrology. The persistent belief of learned men in the relation of stellar conditions to epidemics is in part explained by the fact that astrologers who predicted epidemics wrought charms against the impending pestilence, thus saving their credit, in event the disaster did not materialize, by claiming that it had been averted through their efforts. These primitive views of the origin of epidemics did not necessarily place the cause of the disease outside the earth and its immediate surroundings. Winds, thunder and lightning, fogs, and other meteors were blamed for causing pestilence, and the flight of birds and insects were supposed to be dependent phenomena. Xanaphanes, five hundred or six hundred years before Christ, expounded an idea that the sun was a torch and the stars candles that were put out from time to time. According to his notion, which was seriously accepted, the stars were not heavenly bodies in the wider sense, but meteors thrown off from the earth. So a belief in stellar influence did not carry the mind outside worldly ranges. For this reason other practices than prayers and sacrifices were believed to be effective. They consisted chiefly in efforts to dissipate the meteors, such as huge and numerous fires, and to avoid meteoric influence by confinement in closed or otherwise protected places.

During the period under consideration, the promptings of superstition were paramount and the epidemiologists of the times confined themselves principally to interpreting the signs of the heavens. More advanced views came as the result of reasoning, but the path of discovery by experimental science was not entered upon until after many centuries.

ETIOLOGY ACCORDING TO HIPPOCRATES.

The doctrines of etiology took a more determinate form under the teachings of Hippocrates. According to Hippocrates, disease has its origin either in the régime of life or in the air that surrounds the living body and enters into it. He made therefore a twofold etiological division of diseases, those dependent on the personal régime, and those dependent on the quality of the air. Regarding the latter class, when many individuals are attacked by the same disease at the same time, he supposed the cause to be a common one, namely, the air breathed. Hippocrates believed that a régime of life, which differs with different persons, could not be the cause of a malady that attacks alike the young, the old, men and women. On the other hand, when diseases of different sorts occur, it was clear to him that the cause is individual. Epidemic disease, according to the Father of Medicine, is often promoted by a specific, unknown, and extraordinary condition of the air due to the presence of the *quid divinum*, which may also exist in miasms and certain other impure things. This *quid divinum* has given much trouble to the followers and commentators of Hippocrates, and the judgment as to what he conceived it to be must be left to the fancy of the student of his writings. It seems probable, however, that Hippocrates meant the scourge of divine wrath. It was this very idea that for centuries prevented the application of sanitary measures to epidemic disease. Men regarded pestilence as a punishment inflicted by the Almighty on delinquent humanity and an attempt to turn aside a weapon borne in the divine hand was considered vain and impious.

The influence of Hippocrates's views, with their bearing on sanitation, extended with slight abatement almost to the time when Fracastoro announced his doctrine of contagion. Throughout all this period, moreover, the controlling power of Platonism held experimental inquiry in check. It was believed that the true nature of things could be discovered by the action of reason and not in any important degree by experience and observation. Thus, it will be seen, the measures directed against epidemic disease were often misguided, ineffective, and dependent on all sorts of false doctrines.

GALEN'S VIEWS OF EPIDEMIOLOGY.

Galen, not dissenting from the views of Hippocrates, was of the opinion that any disease that caused the almost simultaneous death of a large number of people should be regarded as of the nature of pest. He did not hold to any view of contagion in these maladies, that is, of their direct communication of man to man, though he evidently believed that the corruption of the air was more intense in the neighborhood of the sick than elsewhere. Pest, he declared, was born of a

pollution of the atmosphere and assailed man by way of respiration. This doctrine was accepted by the pupils of Galen. In the commentaries of the books of Hippocrates on epidemics, or popular diseases, as they were called, it is asserted that pestilential maladies proceed from a special condition of the heavens. These commentaries, at one time attributed to Galen, have since been demonstrated to be the production of his disciples. The long line of Greek, Latin, and Arabic medical writers down to the time of Avicenna, the Mohammedan physician, adhered to the teaching of Hippocrates and Galen, and when they speak of contagion the term must always be understood to mean contracting a disease by breathing altered air. The masters of medicine of the middle ages held similar opinions. Bernardo Gorgonio, professor of medicine at Montpellier, France, in 1300, and Arnaldo da Villanova, who lived toward the end of the twelfth century, gave the name of pestilent fever to every deadly fever and maintained the cause to be a corruption of the air. Guglielmo Varignara, professor of medicine at Bologna in 1302, not only denied the contagious nature of measles and smallpox but declared that the buboes of plague were not contagious. Gentile, who died of pest at Foligno, Italy, in 1348, believed that the poison of pest existed in the air and was due to a putrefaction of this medium. John Godesden, a leading English physician of the fourteenth century, announced the same views. De Chauliac, an eminent French physician of Avignon, who observed the terrible epidemic of 1348-1361, recorded casually his idea that pest could be contracted by contact with the sick, but assigned as a primary cause decomposition of the air due to the conjunction of planets whereby a certain subtle substance is evolved capable of producing epidemics. Another famous physician of those times, Raimondo da Vinario, who was a spectator of the epidemics of pest in 1348-1361 and 1373, says that it is a very dangerous thing to have to do with persons stricken with pest; that one person sick with pest may infect an entire city; that those employed in public hygiene in times of epidemic prevalence take the malady by contagion; that physicians more than any other class are likely to catch the disease; and that monks are generally exempt from pest because they are isolated in monasteries and thus free from outside exposure. Still there is not room to believe that this master of medicine had any precise conception of the nature of contagion. Like so many others, he put his faith in corruption of the air brought about by an influx of stars, planets, and constellations, and in poisonous exhalations emanating from the earth. The danger of contact with the sick he conceived to be due to the air filled with pestilential poison that had been inspired and afterwards exhaled by the victims of the disease. Da Vinario held also that garments worn by the sick and other fabrics in close contact with them contained the infective principle, and hence should

be transported with the sick to a distant and isolated place. Notwithstanding all this, he does not mention the necessity for purification of infected things nor ever suggest the caution of destroying fomites. There can be no stronger evidence than this of the tenacity with which the physicians of the middle ages adhered to the accepted doctrines of their predecessors.

THE BEGINNINGS OF RATIONAL ETIOLOGY.

It took centuries of involuntary observation to shake the idea that epidemics are of celestial origin and to be combated by prayers, fasting, and processions. The first advances toward broader ideas were not made by medical men. The record of reformed views is found in works on jurisprudence and in the narratives of travelers. In the books of jurisprudence of the emperors of the East it is noticed that care should be exercised in having relations with persons arriving from places where pest reigns. It was ordered, in consequence, that those so exposed should be separated from others for the purpose of observation. The term of forty days (whence the word quarantine) is named, this being the supposed maximum period of the duration of acute maladies. Whether this isolation was practiced in a particularly selected place or in the houses of the suspects is not known.

Merchants traveling in the East and detained at Alexandria or Cairo during the prevalence of pest observed that cloistered monks did not contract the disease. Many of these merchants, exiled by pestilence, staid constantly within the boundaries of their residences, transacting all business through barred windows and from terraces that crowned the house tops. The stubbornness with which medical men held to the doctrine of aerial corruption of celestial origin is shown by the report made to the Marseille government in 1720 by a body of distinguished physicians, in which the condition of the air was pronounced to be the sole cause of pest, the idea of communicability from man to man being absolutely rejected.

One of the most ancient edicts commanding the segregation of sufferers from pestilential maladies had for its authors two laymen, Sagacio and Pietro de Gazata, and is found in the chronicles of Reggio d'Emilia. The document, dated 1374 and written in low Latin, orders that all persons sick with pest be taken outside the city, into the open country, a camp, or the woods, there to remain until dead or cured. The parish priests are required to promptly report all cases of pest under pain of death by fire. After registering these historical facts, the chronicler adds:

And I saw in this same year that these orders were observed in Reggio, for which cause all were grieved and terrified more than by the fear of the illness which, when God permits, can not be averted.

ORIGIN OF THE DOCTRINE OF CONTAGION.

The credit of having created the doctrine that pest is contagious by contact with the sick and their effects is chiefly due to Jacobo della Torre, known also by the name of Jacopo da Forli, from the name of a city in central Italy, where he was born in the second half of the fourteenth century. Contagion had been referred to obscurely and timidly from Aristotle down, but now the idea took a practical form. The old notion was that fomites were a sort of tinder that caught from the air an infection existing independently of the sick. Many writers, including Galen, believed there was an extreme degree of atmospheric pollution in the vicinity of the sick, rendering such neighborhoods dangerous, but this was considered a primary cause of the illness rather than a direct emanation from the sick.

Della Torre's doctrines were not accepted by the various schools of medicine and were for a time absolutely forgotten. Fracastoro proclaimed the same theories at a later period, when they were better received, and to him is generally given the honor of announcing the theory of contagion. Jacobo della Torre advised the magistrates of his native town to remove outside the city all persons affected with pest and to isolate them, as well as all persons who had been with them. The authorities were warned against delay, for it was avowed that every precaution would be futile should the disease become diffuse throughout the city. In his recommendations no mention is made of purification, but he asserted his disagreement from the accepted belief in the stellar origin of the infective principle. Della Torre's disciple, Michele Savonarola, attained greater eminence than his master, and so far vindicated the honor of his school as to declare that even persons in good health may transport the pestilential virus to distant places, and that those who are not brought in association with the victims of pest or with pest-bearing things escape the disease. But Savonarola did not fully indorse the teachings of his preceptor. He could not shake off a belief in astrology and admitted that the origin of pest resided in a disorder of the air generated in consequence of planetary contact.

Giovanni da Concorrezzo, toward the second half of the fourteenth century, was so profoundly convinced that pest came exclusively from universal aerial pollution that he denounced as useless every precaution to check the advances of the disease and affirmed that all measures designed to avert contagion are inefficacious.

At this period, when the world had about decided that in epidemics sanitation was not worth while, three observing men lent their influence to broader views and thus gave a potent stimulus to the doctrine of contagion. These writers were Alessandro Benedetti, Marsilio Ficino, and Gerolamo Fracastoro.

BENEDETTI AND FICINO.

Alessandro Benedetti, anatomist and military surgeon, wrote a treatise on pest, published in the last decade of the fifteenth century, in which is presented a résumé of his doctrine concerning pest. Pest, he declared, is not only catching by contact with the sick, but by fomites. The latter, he believed, are capable of receiving and preserving the contagion for long periods. Convalescents from pest, and the things that have been in relation with them, should, he said, be purified before being brought in touch with healthy persons.

Marsilio Ficino was born in Florence in 1433, and passed his childhood in the court of Cosmo de' Medici. He was a priest as well as a physician. Pest had, in Ficino's time, tormented Tuscany, and in 1479 broke out in Florence. The Grand Duke Cosmo de' Medici requested Ficino to prepare a book treating of the pest with the scope of instructing the people how to protect themselves from the scourge. The book, published about 1480, was written in Italian. In writing it, Ficino was associated with Tommaso del Garbo, Mengo da Faenza, and others, and the volume bore the title of Counsel Regarding the Pest. The book is a rare one in its original tongue, but fortunately was translated into Latin and is still preserved in different libraries. The list of the works of Ficino refers to this treatise by the title of *Antidotus*, and it is so cited in many medical books printed in later years. The theories given in this work as to the origin and nature of epidemic disease are the same fantastic stuff that antecedent writers dealt out, but the ideas as to how the disease may be imparted are of a much better sort. The view is advanced that pest can be communicated from man to swine, and that cats and dogs convey the disease. The reader is informed that pestilential poison may abide in the air for long periods and may infect food. Advice is given to boil all drinking water, or to impregnate it with iron rust; to dilute wine with water so prepared; to add an acid sauce to the food; to choose dry food and fruit grown in balsamic and elevated regions, and to dwell on hills or in the mountains. Treating of prophylaxis and dietetics during times of pest, there is a long list of injunctions relative to exercises of the body and the quality of the food. For example, it is enjoined to shun the heat of the sun and of fires; to avoid sweating and the drying of sweat on the body; not to eat fish, or if needs be, to eat small fish from some clear running stream with a rocky bed, and to fry them in oil and treat them liberally with lemon juice, pepper, and cinnamon; and, lastly, there is an enumeration of fruit and vegetables to be chosen or avoided. Overeating and overdrinking are admonished, and it is advised to cook all meat well and prepare it with aromatic condiments. To preserve the health of those in attendance

on the sick, it is directed to keep as far apart as may be from the bedside; to ventilate the sick rooms; to fumigate the house with burning terebinth wood; to carry in the hand a firebrand, a pot of lighted charcoal, or a sprig of rue, mint, sage, or myrtle; and to bathe the body, morning and evening, with warm vinegar. Directions are given to sprinkle the house with preparations of terebinth, juniper, sandal, rose, rosemary, laurel, and similar herbs. The reader is informed that walls, partitions, and all structures made of wood are capable of preserving the contagion for more than a year, and that their disease-bearing qualities should be corrected by washing, fumigations, and fire; that garments of wool and similar stuffs, if not exposed to the air and sun, fumigated often, and well washed, may still contain contagion after three years. The statement is made that the morbid principle can diffuse itself through division walls and enter neighboring habitations. Caution is prescribed in moving animals, money, furniture, and bundles from place to place because of the danger of conveying disease.

FRACASTORO AND SYPHILIS.

Gerolamo Fracastoro is generally credited with being the author of the theory of contagion, but, as has been seen from a review of the works of previous writers, it can only be claimed for him that he elaborated the theory, presented it in a popular form, and lent to the idea the influence of his high authority.

An important event at this period of history was the extensive prevalence of syphilis in Europe, a spread of the disease that gave it every likeness to a general pestilence. The chroniclers of this occurrence were convinced that the disease could propagate itself at a distance, and that it could be communicated by intercourse not more intimate than conversation and social commingling. The malady diffused itself through all classes of society, and history names a king and other potentates among the victims. In Italy the belief prevailed that the disease had gained access to the country with the invading army of Charles VIII, of France. The Italians called it the "morbo Gallico." In France it took the name of the Neapolitan disease. Wide credence was gained by another theory to the effect that the malady had come in by sea with the naked savages of America. In this case it must have spread and taken root very speedily, for it is said that when Columbus went to Barcelona on his way to pay homage to Ferdinand and Isabella, of Spain, syphilis flourished in that seaport; public prayers were being offered as in times of pest, and precautions were being taken against the disease as in case of leprosy.

Laws were made in France for the regulation of syphilis. By an act of the Senate at Paris, dated March 6, 1496, persons affected with

the disease were forbidden under pain of the halter to have any dealings with well persons, and it was ordered that the sick should be segregated in places set aside for their reception in the Faubourg St. Germain. Notwithstanding the rigor of the ordinance, many stricken persons eluded the vigilance of the sanitary guards and moved about in the city of Paris, thereby spreading the disease. The provost then found it necessary to make public cry, warning all persons that thereafter pretensions of ignorance would be disregarded by the authorities, and any individual, native or stranger, afflicted with syphilis and found within the city would be summarily cast into the river and left to his fate.

Some years later there was similar trouble in the Italian part of the Tyrol, trouble which so interfered with one of the most important ecclesiastical gatherings of the times that Pope Paul III, by advice of Fracastoro, removed the Council of Trent to Bologna. Fracastoro had previously written a dignified and graceful medical poem, in Latin, entitled "*Syphilidis sive Morbus Gallicus*," after whose hero, the shepherd Syphilus, the disease received its name.

His interest in this prevalence of syphilis influenced Fracastoro to publish, in 1546, the work "*De Contagionibus*." The great feature of this writing is the presentation of the subject in such a catching way that it took hold on the popular mind, and even had decided effect in loosening the deep-rooted medical opinion of the times. The lesson of contagion was taught by a number of clever similes. For example, Fracastoro divides contagious diseases into three classes, namely, disease catching by contact, in which he compares the mode of communicability to the way in which one decayed fruit spoils another perfect one; disease carried by fomites, a process likened to the persistence of soot on a smoky wall; and disease conveyed to a distance, in which manner the virus is carried just as the volatile essence of garlic or of an onion is borne through space, affecting the nostrils and causing the eyes to water. Fracastoro taught that the poison of disease consists in corpuscles, and that it affects first the minute particles of the animal body. He says that this poison persists in the body, in fomites, or in the air, in proportion to a kind of stickiness existing between the conveying medium and the poisonous corpuscles; and that woolen fabrics and the like absorb, retain, and transport contagion with ease, because they contain interspaces to lodge the corpuscles, and are of a nature to protect the poison from the light, heat, cold, air, dampness, and other conditions injurious to it.

So we see that, with the acceptance of the views of Della Torre, Benedetti, Ficino, and Fracastoro, things were fairly in the way for a beginning of quarantine on a practical basis.

MARITIME QUARANTINE.

Maritime quarantine originated in connection with the Levantine trade. Its early history is associated with that of shipping in the Mediterranean, especially with that of the traffic of Venice, Genoa, and Marseille. Although commercial activity in these waters was initiated by the Phœnicians, the maritime pioneers, records of disease introduced by sea are not found bearing earlier date than the period when Roman navigation was well established. As has been seen, the practice of isolation was first applied against communicable disease by the Hebrews, but their lazarettoes, it appears, were little used in connection with foreign trade, leaving out of the question commerce by sea. In the exchange of commodities with foreign countries the Hebrews were largely dependent on the Phœnicians and Arabs. Had the Jews been active in outside commerce, we should probably read in the Old Testament of sanitary laws applicable to caravans and vessels.

As has been already mentioned, Pliny implies that leprosy was introduced into Europe by Pompey on his triumphal return from the East. It is altogether probable that the Roman ships, laden with spoil from Syria, and bringing many prisoners of war to Italy, carried in leprosy.

In connection with the question of the first recorded introduction of disease by sea a curious error has entered into writings on the subject. J. Freind, adducing evidence in his *History of Medicine* that Procopius was a physician, quotes a translation of Procopius's works by Dr. Howel, and says that the great Byzantine historian describes the pest at Constantinople (A. D. 534) as having originated at Pelusium, in Egypt. This is indeed what Procopius wrote. But it happens that later writers—evidently reading Freind's history—say that Procopius states the epidemic in question was carried to Constantinople by ships and that this invasion of disease became later the foundation of the quarantine establishments on the Mediterranean coast. It is, however, true that the Italian epidemics of the sixth century began in the maritime towns and thence spread inland; but it does not follow that the writers of the time considered the intervention of ships essential to the introduction of disease by sea. For example, Francesco Alfano, professor of medicine at the University of Salerno, which in those days was reputed to be the greatest medical school in the world, writing in 1577, says that the corrupt air capable of introducing pest may be blown over sea and land for long distances; otherwise how could it be explained, he asks, that pest was transported from Ethiopia to Athens and to all Attica? It was considered, moreover, that a ship might easily be pestridden. Even by going to sea a vessel with all well aboard at the time of departure could not always escape the

scourge. The infection extended over the water. Matteo Villani, of Florence, writing in 1581 of the epidemic of 1346, which spread from Asia into Turkey, Egypt, Russia, Greece, and Italy, says that in those evil days numbers of Italian galleys flying from the pest left the stricken ports for healthier harbors. Their crews perished miserably at sea. Some reached Sicily, Pisa, and Genoa, and the disease went with them.

EARLY MARITIME SANITARY LAWS.

There is but little known of ancient laws relating to maritime commerce, and even this little was lost to the world until 1147. The story is an interesting one. Justinian, during his reign, confided to ten jurists the task of collecting and adjusting the numerous Roman laws, together with the various sentences and rulings of judges and magistrates. A compendium of these documents and of the laws promulgated during the rule of Justinian was published. It is known by the name of the *Codex of Justinian*. The only part of this code that treats of ships is called the *Digestum*, and it was lost for hundreds of years. Finally, in 1147, the papers were discovered at Amalfi and made public. The *Digestum* treats of the reciprocal rights of the owners and renters of ships, but no mention is made of sanitary matters. During the long period when this important legal instrument was lost, the Venetians, Genoese, and other Latin maritime nations supplied the deficiency in part from the initial sources of Roman law and in part by custom and agreement. Of this sort are two collections, one known by the name of *Recognoverunt Proceres* and the other called the *Consolato del Mare*. Besides these, there is a great number of documents, such as constitutions, decrees, ordinances, sentences, and the like, which pertain to maritime rights. It is a remarkable fact that, notwithstanding the detailed attention given to most maxims relating to shipping, the *Recognoverunt* and the *Consolato del Mare* are silent too on the subject of sanitation. Therefore, in the Middle Ages, in event of contagious prevalences, it rested with each individual city or country to make such provisions as were deemed opportune. Such an edict is the one, said to be the most ancient of its kind, already mentioned as having originated at Reggio d'Emilia, in 1374, and commanding notification and segregation of cases of plague.

The Venetians were, it is generally admitted, the first to make provision for maritime sanitation. As far back as the year 1000 there were overseers of public health, but at first the office was not a permanent one. The incumbents were appointed to serve during the prevalence of an epidemic only. The first information we have of this kind of public office is under date of 1348, when Nicolaus Venerio, Marinus Querino, and Paulus Belegno (their Christian names given in the Latin of the text) were appointed overseers of public health.

These officers were authorized to spend public money for the purpose of isolating infected ships, goods, and persons at an island of the lagoon. A medical man was stationed with the sick. As a later result of these arrangements, the first thoroughly constituted maritime quarantine station of which there is historical record was established in 1403 on the island of Santa Maria di Nazareth, at Venice. The island had previously belonged to the hermit monks of the order of St. Agostino. The record of the foundation of the first maritime quarantine is found in a Venetian manuscript written by Giovanni Tiepolo, a patrician. The chronicle reads:

1403. The pest began at Venice. A place for a lazaretto was seized from Friar Gabriel, of the order of Hermita, and Santo Spirito was given to him.

Neighboring States engaged in commerce in the Mediterranean speedily followed the example of Venice. The first maritime quarantine station at Genoa was founded in 1467, and at Marseille in 1526. The Marseille quarantine, one of the most complete of its kind, occupied the island of Pomique. This establishment had, in former times, been a leper house, but, in 1476, was converted into a plague hospital, and later became a maritime quarantine station.

It was not until 1459 that a public bureau of sanitation existed in the Republic of Venice. In that year officers, called conservators of sanitation, were regularly appointed. This information was handed down by a contemporary seafarer, Ser Domenico Malipiero, a Venetian patrician, an expert in commerce and diplomacy, who, in 1488, commanded the men-of-war under Captain-General Ser Jacopo Marcello at the celebrated naval battle of Gallipoli. In the contest against the Ottoman fleet the captain-general was killed, and Malipiero (who had a grade relative to that of vice-admiral at the present time) took command and was victorious. Malipiero wrote certain annals of his life which he bequeathed to his son-in-law. This interesting diary, in Venetian dialect, remained secret until 1844, when it was published in the Italian Historical Archives.

The city of Barletta became at one period of the Middle Ages the richest commercial port, next to Venice, in the Adriatic. This was owing to certain concessions granted the city whereby the traffic of a large territory was compelled to enter and leave by her gates. The privilege was not without its drawbacks. Barletta underwent three pestilences of a particularly aggravating character. The first, in 1384, was a strange malady that caused the sufferers to lose their skins like a molting snake. The other two epidemics (1498 and 1656) were probably bubonic plague, and in the last 35,000 souls, almost the entire population of the city, perished. These afflictions gave rise to the practice at Barletta of absolutely refusing entry to any infected vessel until the expiration of a long period of observation at a place outside the entrance of the port.

During all this period land quarantines were in operation at times of pest. Offenses against quarantine, both land and maritime, were severely punished. Pietro Follerio, a great Neapolitan juriconsult of the sixteenth century, mentions whipping, the mill, exile, and death as penalties for infringement of sanitary regulations. A quarantine proclamation and command made by Don Carlo d'Aragona imposes rigorous punishment for surreptitiously entering the city of Palermo during a prevalence of pest. Torture, long service in the galleys, and work among the sick in a pest hospital are named among the penalties. Even the nobles were subject to heavy fines and long imprisonment in the castle.

BILLS OF HEALTH.

Sanitary bulletins were incident to quarantines and cordons. They were so called because they were stamped with the "bollo" or seal of the authority issuing them. When the system of sanitary bulletins was fully developed these patients, in their connection with ships, were designated as clean, when beyond suspicion; touched, when from a noninfected place in active communication with infected places; suspicious, without sickness aboard, but having received goods from places or from ships or caravans from places where pest prevailed; and dirty, when from a place where disease existed.

Professor Bo, a member of the council of health of Genoa, in making researches relative to ordinances of sanitation proclaimed in France in 1850, found an interesting document in the archives of the "Conservatori di Mare di Genoa," a body of officials to whom in mediæval times was confided the vigilance over public health. This writing, dated 1300, makes mention of bulletins of health (*bullettones sanitatis*) with which ships from the littoral of Corsica and Sardinia were required to be provided. Prior to 1300 there is a record in a rubric of the statutes of the city of Urbino, Italy, in which, referring to precautions against pest, it is written that no person shall leave the gate of the city without a proper bulletin, and that, to this end, watch shall be kept day and night at the city gates and walls. During the pest at Naples, in the year 1557, citizens, usually merchants, were stationed at the gates of the city to examine bills of health. Corruption and lack of diligence on the part of these persons were punishable by death. Sentinels, some on foot and some on horseback, made a patrol about the city walls to prevent clandestine entrance. Bills of health to be acceptable had to be stamped with the seal of the university of the place from which the traveler came. They gave not only the day but the hour of departure, together with a description of the traveler. Sanitary bulletins were also issued to accompany merchandise, but in times of severe pest all articles except aromatics and medicaments were considered suspicious. The facts here given are

taken from the instructions written by Pietro Follerio, an eminent jurisconsult, who was assigned by the viceroy of Naples to superintend the province of Campania during the prevalence of pest with the special duty of indicating means for the betterment of public hygiene. It is worthy of notice that the provisions of public sanitation in those times are usually found, not in books of medicine, but in treatises on jurisprudence. This is explained by the fact that the medical profession was looked to for scientific indications only, and that the application of sanitary measures founded thereon, limiting or compromising as they often did the rights of the public or the constitutional privileges of citizens, was a matter for legal consideration and action.

AN EARLY SANITARY CONGRESS.

The efforts of some of the pioneers of quarantine were at times ill-advised, did not always meet with general approval, and sometimes, indeed, occasioned strong outbursts of popular indignation. The experience of Girolamo Mercuriale (called the *Æsculapius* of his time) and of his colleague Capodivacca is an instance. In the summer of 1576 the frequency of strange febrile diseases, often very mortal, was observed at Venice. The supreme magistrate of health of the Republic of Venice, suspecting pest, called a conference of great physicians, among others Girolamo Mercuriale, Capodivacca, and Nicola Massa. As for the verdict Massa wavered, and the other members were divided into two camps, one body for and the other against pest. Mercuriale and Capodivacca asserted decidedly that the malady was not pest, but an epidemic of fever, due to the excessive heat of the season. This opinion carried the day, and no precautions were taken against the spread of the disease. Unfortunately for the optimistic diagnosticians, the illness increased, and speedily took on all the characters of pest. The populace uprore and made an effort to lynch Mercuriale and Capodivacca and burn their houses. Both the physicians, fortunately for them, escaped by flight, their property being saved by prompt action of the authorities.

EARLY EFFORTS AT DISINFECTION.

The armament of disinfection in early days was full of oddities. In the process of purification time was more trusted than anything else. Gian Filippo Ingrassia, appointed by Philip II of Spain to establish a public sanitary service in Sicily, begins his book on pest and contagious disease with the following distich by Martello:

*Lana, aura et linum captant contagia pestis;
Ignis, furca, aurum sunt medicina mali.*

Before reviewing the different means besides fire, the gallows, and money used against contagion, it is interesting to make a survey of

the things, in addition to wool, the air, and garments, that were reckoned infectible. Animals were considered capable of conveying disease. During the pestilence at Palermo in the year 1575 Ingrassia caused all the dogs in the city to be brought together alive on a certain day and cast into a common pit, where they were covered with quicklime and then with earth and stones. As to cats, they were allowed to live, so as "not to have worse war with rats," says Ingrassia, but all cats that had been near suspected houses were required to be kept closed up. There were similar restrictions for fowls and pigeons. Elsewhere geese and cattle were banished from the cities during epidemics. Habitations, ships, and even the sails and cordage with which vessels were rigged belonged to the category of infectible things. Nicola Massa, a Venetian physician, who published in 1556 a book on pestilential fevers, names the following as fomites: Wool, hair, cotton, linen, hemp, silk, thread, and all things made from these substances; skins, feathers, and the like; and all merchandise, as well as sacks, baskets, boxes, casks, and cords that cover them. Massa considered as noninfectible all metals and objects made of them, including arms and cooking utensils; precious stones and marble; grain, flour, and meal; vegetables, fruit—fresh and dried—and nuts, wine, oil, and vinegar; and all drugs and aromatics. In regard to metallic money he said that those who held it in suspicion might allay their fears by receiving it in a vessel of vinegar.

Exposure for many days to the air in selected places and to the dew was looked upon with great favor. The dew of the dead of night was supposed to be particularly efficacious. This practice originated in the more or less accurate observation that during the season when the mists of the Nile were thickest the pest in Lower Egypt began to diminish.

The vapors of volatilized aromatic substances, known technically as "perfumes," were credited with great virtues in correcting the alteration of the air generated by pest. Cloves, cinnamon, cedar bark, camphor, mints, resinous wood, and similar substances were kept boiling in pots of vinegar and rosewater for long periods. One recipe containing garlic and known as the "vinegar of the four thieves" enjoyed high repute. Fumigations in summer differed from those in winter. Aromatic wine was added in fumigations for cold weather, being assumed to have a special property of correcting air at a low temperature. It was also considered advisable to lengthen the period of isolation in winter because cold was thought to have a tendency to conserve the contagious principle. Sulphur fumigation was not regarded with favor in early days. The strong sulphurous fumes were said to alter the air unfavorably rather than rectify it; but sulphur came more into vogue in the eighteenth century. The burning of gunpowder was also thought useful.

Huge fires, kept burning for weeks, were used from the most ancient times. The physician Acron is reputed to have rendered great service by the use of fires at Athens during the pest at the beginning of the Peloponnesian war. Fires made of shavings and chips were thought preferable, because they produce a clear flame, without smoke. Aromatic wood was added to these fires, but special caution obtained against burning anything producing an offensive odor, such as the wood of certain nut trees, for fear of liberating vapors likely to add to the disturbed condition of the air. Not only were garments and similar articles burned, but sometimes houses and ships as well. Opposition often existed against such measures on the ground of further deteriorating the atmosphere.

Mixtures of lime were favorably regarded and whitewashing of infected apartments was habitually practiced. Acid fumigations are spoken of in the eighteenth century. Muriatic acid fumes, suggested as a disinfectant in 1774 by Guyton Morveau, of Paris, were used in 1800 to disinfect rooms, garments, mattresses, and the like, after the epidemic of yellow fever in Spain ("Yellow fever in Spain," Yellow Fever Institute, United States Public Health and Marine-Hospital Service, Bulletin No. 5). With all these measures, great stress was laid in cleaning up infected cities during and after epidemics, giving special attention to sewers, wells, cesspools, and disposing properly of dead bodies. In reading the chronicles of the middle ages the conviction can not be avoided that, were it not for occasional epidemics, public sanitation would have fallen entirely into disuse.

MEASURES ADOPTED IN A PEST-STRICKEN CITY.

To gain a precise knowledge of what measures were usually practiced in places afflicted with an epidemic in early days, it is instructive to examine specifically the provisions adopted in a particular city. A suitable instance is presented in the Treatise on Plague, by Alessandro Massaria, who was in charge of sanitary measures at Vicenza, Italy, during a prevalence of bubonic plague of one year's duration in 1577. The first death was attributed to garments clandestinely introduced from Padua, where plague prevailed. After a necropsy establishing the diagnosis the furniture in the house was burned and every exposed person stripped, given new clothes, and removed outside the city. The house was purified by aromatic fumigations and painted with milk of lime. All infected vestments and bedding received a treatment with strong lye. The disease, however, spread, and in one year the city, with a population of 30,000, suffered 1,908 deaths from plague. As soon as the epidemic established itself the city was divided into 32 sections and a daily house-to-house inspection made by 64 trustworthy citizens, two to each precinct. All cases of sickness were reported to one of four public physicians. These physicians served for periods of

fourteen days. Infected habitations received the same treatment as in the initial case, except that the furniture was not burned in all instances, but washed instead with lye and left in the sun and open air for thirty days. All garments were put in running water for two days. Persons exposed or under suspicion went to the Campo di Marte, outside the city walls, where wooden houses had been built. A river separated the isolation camp from the lazaretto, where the sick were lodged and where physicians and nurses were in attendance. Suspects developing plague in the isolation camp were taken across the river to the lazaretto, and convalescents from the latter place were transferred to the former. Those who kept well in the Campo di Marte for twenty-two days returned to their disinfected homes in the city, there to remain under observation for an additional twenty-two days. Convalescents from the lazaretto passed twenty-two days in the isolation camp, and were afterwards confined to their houses in the city for another twenty-two days. At the height of the epidemic all the houses in the city were closed for forty days, and none but the guards were allowed in the streets. At this time 5,000 persons were fed from public funds, and there were about 400 persons in the lazaretto and 500 on the Campo di Marte.

EARLY MARITIME QUARANTINE STATIONS.

The maritime quarantine stations of the sixteenth century consisted of an anchorage, barracks for suspects and convalescents, and a place where purification could be applied. The practice, with obvious modifications, was the same as in the case of an infected city. The personnel of these stations consisted in many places, at the earliest times, of surgeons and their assistants, for plague, being regarded as a surgical disease, did not fall clinically into the hands of physicians. At a later period the physicians conducting the stations were aided by surgeons, barbers, and experts in aromatics, because, as Massa says, the physicians were so limited in their acquirements as not to know how to do manual operations or treat external maladies.

With a view to learning how the various methods of disinfection were practically applied at early maritime quarantine stations, it will be interesting to relate what was done to a Catalan ship that arrived at Palermo from Barcelona on the way to Naples at the time Ingrassia was chief of sanitation in Sicily. The account at least shows that the sanitarians of the sixteenth century were thoroughgoing. This vessel had 97 persons aboard, 18 of them passengers. Three seamen and two passengers had died of a disease suspected of being pest. The deaths occurred while the vessel was taking on cargo in the harbor where she lay at anchor. The cargo consisted of barrels of salted fish, cases of sugar (destined for Palermo, and already disembarked and in

store), salted cheese, salt in bulk, a quantity of sumac, and merchandise, including many bales of cloth from Barcelona, a port not under suspicion. The master of the vessel was at once required to give 20,000 scudi security not to leave the harbor until given pratique. To make assurance doubly sure, the rudder was taken away from the ship and a watch set. All persons, except the sick and a sufficient number of seamen to guard the ship, were sent ashore to a place known as the Borgo, where all garments were taken from them and they themselves exposed to the fumes of boiling pitch and afterwards washed with vinegar. Some of the clothing was burned and some washed, aired, and perfumed for fifty days.

The sick were sent to a lazaretto, the Cuba, a huge stone building, which still stands at Palermo as a monument of early quarantine.

The treatment given the cargo was as follows: Barrels of salted fish, washed outside, first with sea water and then with vinegar; cases of sugar, salted cheese, and sumac, coverings removed and burned and the commodities without further treatment delivered to the owners; salt, no treatment, not being considered infectible; merchandise, aired and perfumed ashore for 50 days, and the cloth unrolled and hung from the rigging of the ship for 50 days. The sails and cordage of the ship were taken down, submerged in the sea for a week, and then hung from the masts, yards, and booms in the air, sun, and dew, by day and night, as long as the ship remained in quarantine. Fumigation was made in the interior of the ship by boiling pitch in caldrons between decks. Fifty days were set as the period of detention, instead of forty, because the season was winter.

FURTHER HISTORY OF QUARANTINE.

Without touching on quarantine in America, which is another and interesting story, it is profitable to take a view of the further history of quarantine in Europe. Following the discovery by Anthony van Leeuwenhoek, in 1675, of bacteria, called by him "animalcules," there was a wide belief in the casual connection of microscopic creatures with disease, a belief supported by the doctrine of living contagion enunciated by Marcus Antonius Plenciz, of Vienna, in 1762, but it was without marked effect on quarantine procedure. The theory, in fact, lost hold on the public and medical minds to such an extent that in the early part of the nineteenth century the doctrine of a living contagion was looked upon as an absurd assumption. It was not until the middle of the last century, following the investigations of Pasteur, Pollender, and Bavaine, that quarantine practice became established on its modern scientific basis.

English quarantine procedure prior to 1800 did not differ much from that of the Mediterranean ports. English vessels, which did

not begin to enter the Mediterranean until the time of the Crusades, were usually, in early years when engaged in the Levantine trade and from infected ports, sent to Mediterranean quarantines for treatment. In 1710, under the reign of Queen Anne, a rigorous quarantine act was passed in England, and in 1721 two ships with cargoes of cotton goods from Cyprus, where plague prevailed, were burned by the sanitary authorities in English waters. A quarantine station was established in 1741 in Stangate Creek, on the Medway. Here vessels, not treated at Mediterranean quarantines, were submitted to practically the same procedures as were in vogue at French and Italian ports. Floating hulks were also used as quarantine stations in England from about the middle of the eighteenth century. The act of Queen Anne's reign was qualified by later enactments, and during the pest in Poland, in 1780, vessels bound for England from the Baltic were compelled to undergo a typical old-fashioned quarantine. A few years later there was an order in effect directing all vessels on the way to England and liable to quarantine to show a yellow flag at the mainmast head when in sight of other vessels at sea during the day and a distinctive light at night. From the beginning of the nineteenth century quarantine restrictions were, by changes in the laws and their application, materially relaxed in Great Britain, and as a substitute for former practice it has not been the custom in modern times to detain any vessel unless there has been communicable disease aboard during the voyage, or such exists on arrival. Following the decision of the Spanish Government in 1821, that yellow fever was to be considered quarantinable, an inquiry on the subject was made in England in 1823 and 1824, which resulted in the passage of a law directing the same procedures to be applied against yellow fever as against plague.

In France, until the year 1821, vessels from the Levant were not allowed to enter at any ports except Marseille and Toulon. The sanitary regulations of these ports were fortified by royal edicts. With the appearance of yellow fever on the frontier of Catalonia in 1821, an appalling epidemic that spread from Barcelona and killed 25,000 people in five months, a law was passed by the French Chambers, March 5, 1822, making a uniform sanitary code for all France, which, with certain subsequent modifications, formed the basis of French maritime sanitary practice.

Quarantine in the different continental European maritime countries during the eighteenth century was practically on a uniform basis, and during the first half of the succeeding century quarantine was practiced on the same lines in all European countries engaged in Eastern, American, and African trade, England excepted.

The international sanitary conferences at Paris in 1851 and 1852, in which participated the different European powers having interests in the Mediterranean, marked the close of the old régime of quarantine.

Delegates were present from France, Austria, the two Sicilies, Spain, the Roman States, Greece, Portugal, and Turkey. England was not signatory. Regulations were adopted much less restrictive than former ones, it being admitted that the efficacy of many measures formerly practiced was doubtful or negative, science having proclaimed that, for the most part, pestilential maladies are not contagious. This surprising declaration was followed by a revolution in quarantine methods on the Continent and resulted in the general adoption of practices based on the limited communicability of epidemic diseases. These changes, with which the early history of quarantine closes, were brought into effect at the beginning of the new era, during which the doctrine of specific living causes of epidemic diseases have been built up on the substantial basis of experimental medicine.

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YELLOW FEVER INSTITUTE, BULLETIN No. 13.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

REPORT
OF
WORKING PARTY No. 1,
YELLOW FEVER INSTITUTE.

A STUDY OF THE ETIOLOGY OF YELLOW FEVER,

BY

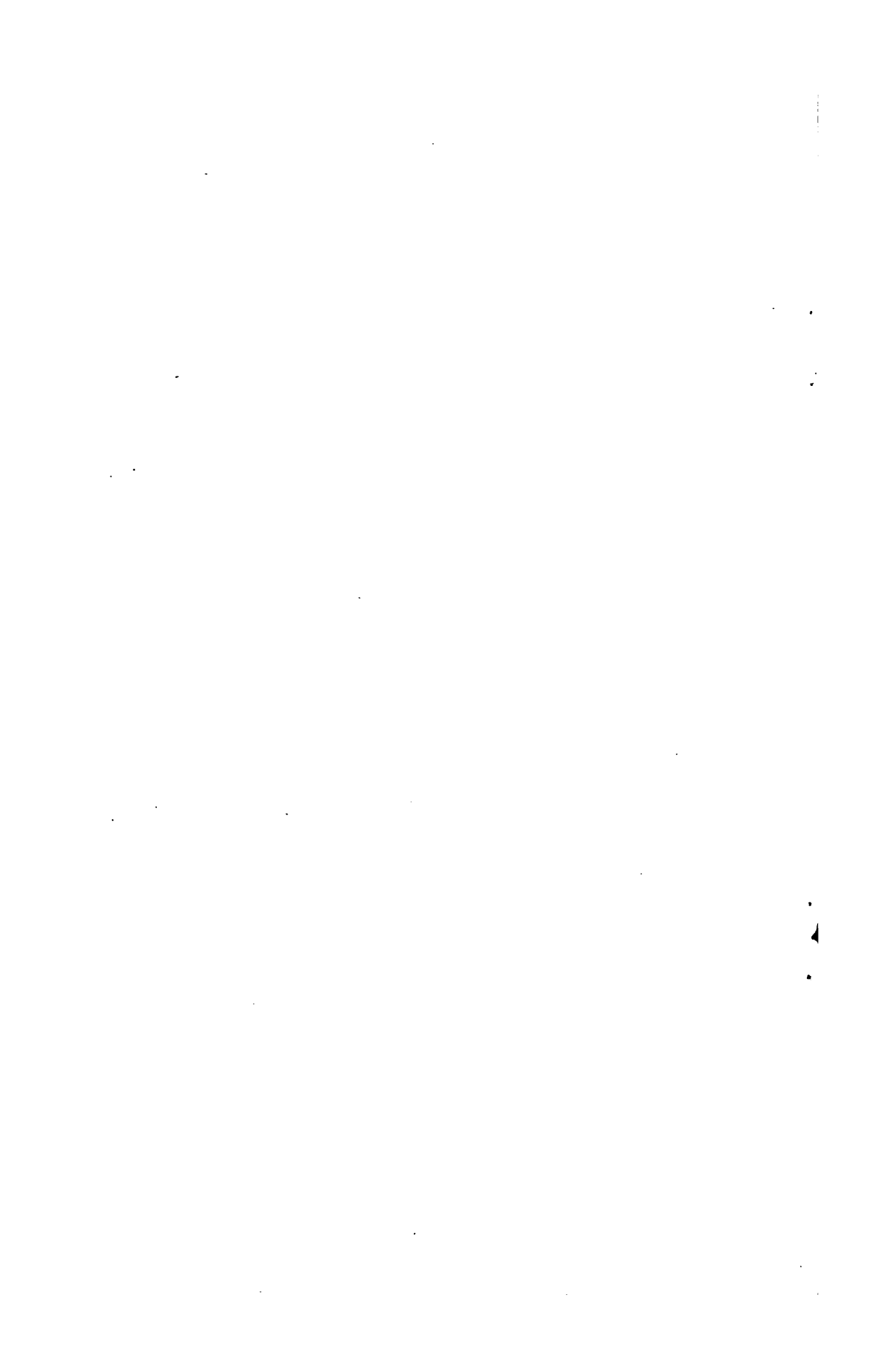
HERMAN B. PARKER, ASSISTANT SURGEON.

GEORGE E. BEYER, ACTING ASSISTANT SURGEON.

O. L. POTHIER, ACTING ASSISTANT SURGEON.

MARCH, 1903.

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GOVERNMENT PRINTING OFFICE.
1903.



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PREFACE.

ORGANIZATION OF WORKING PARTY NO. 1, YELLOW FEVER INSTITUTE.

TREASURY DEPARTMENT,
U. S. MARINE-HOSPITAL SERVICE,
Washington, March 5, 1902.

SIR: Referring to Department approval of September 25, 1901, of the formation within this service of a yellow-fever institute, I have the honor to invite your attention to as much of the plan of organization as says, "The object of the institute is to collect facts concerning yellow fever, to designate specific lines of inquiries, and to make them."

In accordance with this plan and in view of the fact that the etiology of yellow fever seems still to be involved in much doubt, it seems desirable to make further investigations into this subject. With this end in view an officer of the service, Asst. Surg. Herman B. Parker, has been receiving special training in the hygienic laboratory, and it is desired to associate with him Dr. George E. Beyer, professor of biology, Tulane University of Louisiana, and Dr. O. L. Pothier, pathologist to the Charity Hospital, New Orleans, La., who have both made a special study of the transference of disease by mosquitoes and have recently made a report to the Orleans Parish Medical Society (November 30, 1902) on this subject.

In view of the fact that yellow fever prevails to only a very limited extent at the present time, it is not deemed advisable to dispatch this working party immediately, but it is under contemplation to do so as soon as an outbreak of any magnitude occurs in either Mexico, Central or South America.

In order to prepare for this contingency, therefore, I have the honor to request authority, when the exigency arises, to nominate the above-named Drs. George E. Beyer and O. L. Pothier as temporary acting assistant surgeons, U. S. Marine-Hospital Service, for duty in making the above investigations.

This request is made necessary by the fact that Drs. Beyer and Pothier are engaged in the practice of medicine and in teaching in the

Tulane University in New Orleans, and will have to make preparations and arrangements for a prolonged absence from the scene of their present duties.

Respectfully,

WALTER WYMAN,
Supervising Surgeon-General, M. H. S.

The SECRETARY OF THE TREASURY.

WASHINGTON, D. C., *March 6, 1902.*

Approved:

O. L. SPAULDING, *Acting Secretary.*

TREASURY DEPARTMENT,
U. S. MARINE-HOSPITAL SERVICE,
Washington, D. C., April 25, 1902.

SIR: You are hereby relieved from duty in the hygienic laboratory and appointed chairman of a working party of medical officers for the purpose of making scientific investigations of yellow fever, malarial fever, and dengue, and other diseases common to the United States and Mexico.

For this purpose you are directed to proceed to Vera Cruz, Mexico, where, in conjunction with Drs. Beyer and Pothier, constituting the other members of this working party, you will enter upon these investigations.

You will make a monthly report to the Bureau as to the progress of the working party, and upon the completion of the investigations will make full report of the same.

Respectfully,

WALTER WYMAN,
Surgeon-General, M. H. S.

Asst. Surg. H. B. PARKER,
Hygienic Laboratory, Washington, D. C.
(Through Director.)

YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service,

WALTER WYMAN, Surgeon-General.

BULLETIN No. 13.

Section B.—ETIOLOGY.

P. A. Surg. M. J. ROSENAU, Chairman of Section.

A STUDY OF THE ETIOLOGY OF YELLOW FEVER,

By HERMAN B. PARKER, *Assistant Surgeon*,
GEORGE E. BEYER, *Acting Assistant Surgeon*,
O. L. POTHIER, *Acting Assistant Surgeon*.

1. LETTER OF TRANSMITTAL WITH CONCLUSIONS.

TREASURY DEPARTMENT,
BUREAU OF
PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE,
New Orleans, La., February, 17, 1903.

SIR: In compliance with the Bureau orders of April 25, 1902, wherein a working party consisting of Asst. Surg. Herman B. Parker, and Acting Asst. Surgs. George E. Beyer and O. L. Pothier, working in conjunction with the yellow fever institute, were to proceed to Vera Cruz, Mexico, and begin the investigation of yellow fever and diseases common to Mexico and the United States, we have the honor to state that the working party arrived in Vera Cruz on May 12, 1902, secured quarters for the laboratory and began these investigations. This work terminated about the end of October. Since then we have been studying the material brought to this country and collaborating the notes made in Mexico. This work is concluded and we have the honor to present the report of the investigation.

We have to acknowledge the assistance and encouragement from every officer of the Mexican Government with whom we came in contact, whether directly or indirectly connected with the department of medicine. We especially acknowledge the courtesies extended by

Governor Dehesa and his staff of the state of Vera Cruz and by Dr. Eduardo Licéaga, president of the superior board of health of Mexico. Through them every channel was opened for the proper study of the disease.

To our daily companions, Drs. Matienzo, del Rio, and Iglesias, a commission appointed by the Mexican Government to associate with and assist us with their valuable clinical experience, we are indebted for suggestions and their uniform interest shown in the work.

In the proper study and classification of this new parasite, the working party desires to express its thanks to Mr. J. C. Smith, of New Orleans, La., for valuable aid and suggestions in working out the life history of the organism.

The United States Consul, Mr. W. W. Canada, and Acting Asst. Surg. S. H. Hodgson, United States Public Health and Marine-Hospital Service, were untiring in their efforts to make this work a success and to them we are indebted for much assistance. To Mr. Alexander M. Gaw many thanks are due for his interest in procuring and selecting the experimental material.

Following are our conclusions: 1. That the bacteriologic examination of the blood of cases of yellow fever during life and the blood and organs at autopsy performed immediately after death in uncomplicated cases is negative.

2. That *Stegomyia fasciata*, when contaminated by feeding on a case of yellow fever forty-one and a-half hours after the onset of the disease and subsequently fed on sugar and water for twenty-two days, one and a-half hours, can, when permitted to feed on a nonimmune individual, produce a severe attack of the disease.

3. That *Stegomyia fasciata*, contaminated by feeding on a case of yellow fever and after varying periods killed, sectioned, and appropriately stained, presents with regularity a protozoan parasite, the *Myzococcidium stegomyiae*, that can be traced through a cycle of development from the gamete to the sporozoite.

4. That *Stegomyia fasciata* fed on blood from a case of malarial fever, on normal blood, or artificially fed, does not harbor the parasite indicated in conclusion 3.

Respectfully,

HERMAN B. PARKER,
Assistant Surgeon,
GEORGE E. BEYER,
Acting Assistant Surgeon,
O. L. POTHIER, M. D.,
Acting Assistant Surgeon.

The SURGEON-GENERAL,
U. S. Public Health and Marine-Hospital Service,
Washington, D. C.,
Chairman Yellow Fever Institute.

2. PRELIMINARY.

A.—THE OBJECT OF THE WORKING PARTY.

It is almost unnecessary to review the influence that yellow fever now exerts over the economics of that part of the United States that borders on the South Atlantic and Gulf seaboard. In past years the experience was that in certain seasons of the year no city on the whole Atlantic seaboard was exempt from yellow fever, as the great epidemics of Boston, New York, Philadelphia, Baltimore, and Charleston testify. With the advancement of sanitary science, however, the disease crept slowly southward until it is now outside the confines of the United States. There now remains what is called "infectible territory;" that is, territory which, if the disease is introduced, furnishes the medium for the propagation of the disease. According to the quarantine laws, this territory includes all of the United States south of the southern border of the State of Maryland. In the light of recent investigations, it includes all that territory where the mosquito, the *Stegomyia fasciata*, finds its natural breeding place. The cities and towns in the United States where the insect thrives have not been accurately tabulated; from an epidemiological point, it would not be necessary or wise to make such a classification, except as a matter of interest, of more importance is it to study those towns that furnish the natural breeding places for this insect, for, should it be absent for the time being, there is always the danger of introduction through commercial channels from one of the centers of distribution, and establishing a habitat in a season or a part of a season.

Broadly speaking, that which constitutes a natural breeding place for this insect is the house, town, or city that stores its water supply in small unprotected containers for daily consumption during the period of flight, i. e., from March to November on our Gulf coast. These conditions supplied, there only awaits the time when commerce, either ships or railways, introduce the insect for domestication.

In what part of the United States are these conditions supplied? Beginning with Charleston, on the Atlantic coast, to the Mexican border, on the Gulf, and on the lines of railway and water communication in the interior from the centers of distribution.

All the cities and towns included in the area of infectible territory are not equally incriminated. Charleston, Savannah, and Brunswick now harbor few, if any, *Stegomyia fasciata*. Mobile, with its good

water supply, is rapidly eliminating not only the chances but the danger of infection; Jacksonville, Miami, Key West, Tampa, New Orleans, Brownsville, Eagle Pass, and Galveston now harbor *Stegomyia fasciata* in abundance.

Owing to the character of the water supply or system of the above-mentioned cities they furnish the same natural breeding places for this insect as Cuba, Mexico, Central and South American ports, where yellow fever prevails all the year. Owing, however, to periods of cold during the winter months, the spring and early summer generations are usually not numerous. From the end of August to the first of November they will be found in the same numbers as in the Tropics. There are, however, seasonal prevalences when the insect prevails in great numbers in the early spring months, the same as in more tropical regions.

It must not be forgotten that the species *Stegomyia fasciata* is not a native mosquito in our own country, but is domesticated more particularly in the places mentioned through the medium of commercial intercourse. This fact can not be disputed when the habits and breeding places are taken into consideration, the breeding places not being furnished until the beginning of civilization on this continent.

As a result of the existence of an area of infectible territory, and the prevalence of the disease in neighboring islands and mainland, a quarantine was established whereby ships and passengers from suspicious or infected territory were detained under observation after disinfection for periods varying from five to forty days or longer from the infected place. In recent years the maximum period of incubation of the disease, five days, was selected as the detention period; this continues in force at the present time.

Prior to the year 1900 disinfection for yellow fever approached, as nearly as chemical disinfection would accomplish it, the sterilization of every part of the ship. Steam, formaldehyde, and sulphur were used energetically to accomplish this purpose. This process was in accord with the knowledge of the times and undoubtedly limited the infection in numbers of cases. It did not meet the requirements, however, and infection from time to time was introduced and produced epidemics with varying severity without serious reflection on the quarantine officer, through whom it passed, or his methods of applying the disinfection. When one takes into consideration that the quarantine officer knew nothing of the etiology of the disease which he was striving to prevent, the wonder is that accidental infections were not more numerous than they were. In other words, the same methods were employed as in dealing with plague, cholera, or other quarantinable disease, caused by vegetable organisms, when there should have been employed an efficient insecticide, directed to the destruction of the mosquito.

The statement that disinfection of ships should have been superseded by the destruction of mosquitoes needs a definite explanation. The whole mass of corroborative evidence is that the *Stegomyia fasciata* is the medium for the transference of the disease. This is looked upon as a definite scientific fact. Is it, or is it not, the only means of transference? To prove a negative assertion conditions must be supplied to produce the disease at will or under constant conditions. In the whole history of the disease such data, to this date, are wanting. When one instance occurs and can be repeated the new factor can then be taken into consideration.

Knowing, then, as we do, that an individual sick with the disease harbors the infection in his blood, and that a mosquito which has bitten such a case can, after a period, carry the disease to a susceptible individual through the act of feeding, there remains to be found the cause or organism that is the infecting agent.

What advantage is to be derived by knowing the cause of the disease? There is nothing of more importance to the commerce of the whole United States, and especially our Southern States, than to say definitely that the cause of the disease is, or is not, a *protozoan* parasite, and that there is a demonstrable cycle, either in one or the other host. Once demonstrated, the two go hand in hand, as the whole biologic evidence supports the assertion that in the conveyance of protozoa by animal life, but one genus is the rule in such transference. It will be seen, then, that there is a biologic basis for the one medium of contagion, and that efforts for the eradication, transference, prevention, or quarantine would be applied to but two factors—the individual sick with the disease and the genus *Stegomyia*.

The chief aim of the working party was the identification and classification of the specific organism of yellow fever. It was our intention to use every legitimate means to accomplish this end without producing suffering or pain to those under the influence of the disease or in any experimentation that we should deem proper. The bacteriological theme had been well worked over; for our own information it was to be gone over again, especially during the period when the disease could be transmitted to the mosquito.

The blood was to be examined with all modern reagents before the advent of and during the course and convalescence of the disease. All tissues were to be examined histologically after post-mortems to see if they contained either within the cells or in the intercellular substance any organisms or foreign body to which the etiology could be identified. Mosquitoes were to be contaminated by feeding on well marked cases and at varying periods killed and sectioned for histological examination, to determine the presence of a developmental or cycle of maturation of an organism belonging to the *Sporozoa*, and upon the identification of such an organism to give a practical demonstration of its intimate association with the etiology of the disease.

All of this ground had been well worked over by some of the best men of the age with unfruitful results, yet it seemed to us that one technique or another would reveal what we were striving to find; that it was more a question of technique and recognition of something noted before than an actual demonstration in the blood of some organisms that had escaped observation.

An accurate study of the life and habits of the *Stegomyia fasciata* was to be worked out, giving in detail its connection with yellow fever. The other mosquitoes present in Vera Cruz were to be classified and studied in their relation to disease. Such facts of importance that bore directly or indirectly upon quarantine were to be noted and reported.

The result of this work is classified serially.

B.—SANITARY HISTORY OF VERA CRUZ.

The earliest record that we can find showing the presence of yellow fever in Vera Cruz was in 1509, when Diego de Nicues occupied the place, then called New Spain, with 780 men. On the first days of the occupation they lost 400 men; shortly afterwards 200 more; at the end of fifteen months there remained only 60 survivors. From that date the fever has probably continued with variations that correspond to the supply of nonimmunes. The early historical data deals only with great epidemics and correspondingly great losses of life.

During the last thirty-six years, a more or less accurate system of vital statistics has been kept. It is surprising to note that during this time 7,861 deaths have been ascribed to this disease, occurring annually as follows: Estimated population, 38,000.

Year.	Deaths.	Year.	Deaths.	Year.	Deaths.	Year.	Deaths.
1866.....	264	1876.....	34	1886.....	208	1896.....	0
1867.....	332	1877.....	528	1887.....	4	1897.....	2
1868.....	187	1878.....	448	1888.....	3	1898.....	127
1869.....	10	1879.....	21	1889.....	2	1899.....	670
1870.....	11	1880.....	254	1890.....	40	1900.....	259
1871.....	271	1881.....	723	1891.....	180	1901.....	102
1872.....	215	1882.....	72	1892.....	259	1902 (to July 1).....	115
1873.....	322	1883.....	747	1893.....	131		
1874.....	79	1884.....	136	1894.....	209		
1875.....	425	1885.....	328	1895.....	143		

During the six months ended June 30, 1902, there were reported 115 deaths from yellow fever, more than one-half of which occurred during our residence there in the last two months. In the month of July there were 30, in August 41, and in September 28 deaths from this disease. Our investigations practically ceased at the end of September.

It would not be amiss to give a general description of the city, with reasons why it has always been a center of infection. Until the last few years the city was built up to within one block of the sea wall.

Three years ago this wall was extended about 200 yards, and on the north carried across the channel, thus connecting the island of Ulua with the mainland, and forming an admirable breakwater for the heavy north seas that break over that coast during the winter months.

The city proper is built as all tropical American cities are. The houses have thick walls, dimly-lighted interiors, and a "patio," or courtyard, in the center. The newer part of the town, where the poor people live, is built mostly of wood and lies to the south of the main town. The sewerage system is primitive, each house or "patio" having a cesspool for the collection of solid excrement. The drainage system for the entire city is superficial; all fluids from the houses and streets run into an open gutter in the center of the street and slowly flow toward the Gulf. The fall of the city is about 4 feet, with the incline toward the Gulf.

The water supply is in keeping with the sewerage system. Many of the older houses still retain their cisterns in some part of the "patio," either exposed or loosely covered with boards. Others have connections with the small water mains, but the great majority, especially those houses occupied by the poorer classes, have no water supply except that caught in barrels and tanks during the heavy rains, or the water from the public street taps carried to the houses in small cans and stored in some convenient uncovered receptacle for the family use.

It will be seen that every house has either one large cistern or a number of barrels and small receptacles, from one to twenty, upon which they depend for the water supply. As we will explain later, the yellow-fever mosquito is purely a domestic mosquito, and finds natural breeding places in such containers. It was an invariable result that an examination revealed from several to many thousand larvæ in every uncovered barrel or tin can. The large cisterns, situated below the ground, gave very few, if any, larvæ. This is accounted for by the numerous other aquatic larvæ and insects that occupy the cisterns, either using the larva of *Stegomyia fasciata* for food, or else a preference of this mosquito for more convenient and better-lighted breeding places.

The social customs of the people are to a large extent conducive to infection and the continuance of yellow fever. The natives of all classes close their places of business and stop work in the middle of the day in order to give their employees about two hours' sleep during the period of greatest heat. This custom is followed by strangers from the day of arrival, and here is the explanation of the immediate infection. The time of flight of the insidious *Stegomyia fasciata* is during the daytime. She finds food in abundance, without resistance, during the hours from 12 to 2, and transmits her infection to all without regard to previous history. Even in Vera Cruz the presence of this mosquito is seldom troublesome, so that the use of mosquito

bars is not demanded or used during the daytime—another factor that aids in spreading the infection.

While the hands and face are usually selected as being the most convenient sites for biting, being exposed, the ankles also come in for a fair share. The use of low shoes and thin socks favor this site, and the practice is condemned as being dangerous during the prevalence not only of yellow fever but also of malaria.

While many foreigners and better-class Mexicans from the “tierras templadas” die annually of yellow fever in Vera Cruz, it may be said that the whole infection is kept virulent and constant by the presence of the native Indians who come down from the mountains to work on the harbor improvements or to sell their native wares. While in Vera Cruz they have no regular domicile, but lodge either in the streets or in large lodging houses, called “patios.” These “patios” are seldom without infection; one alone contributed 17 out of 53 deaths from yellow fever in the city during the month of May. It is the Indian mortality that makes the death rate of Vera Cruz excessive. While strong physically, they are slightly resistant to disease, especially yellow fever.

Malaria probably ranks second, tuberculosis third, on the mortality list of the infectious diseases. The infant mortality is necessarily large, death taking place from intestinal disorders.

Outside the infant mortality, due to general bad hygienic conditions, and yellow fever mortality among the strangers, the city is practically free from infections that are so common in our own country; in other words, if the preventable diseases were modified by concerted action on the part of the authorities, we have no hesitancy in stating that Vera Cruz would be as healthy, if not more so, than our average southern city, and as healthy and far more comfortable than any city on the borders of the Gulf and Caribbean sea.

One can not give a general description of the sanitation in Vera Cruz without noting the immense number of black-headed vultures or buzzards that infest every part of the town. They naturally assist in removing from the streets all particles that furnish food for such scavengers.

We are glad to state that the general and city governments are aiding in every way in perfecting a sewerage system, a water system, and in paving and draining the streets of the city. These improvements are inspired somewhat by the results obtained by our own people in the various cities of Cuba and Porto Rico, and when completed they will assist materially in the general sanitation of the city. This work is expected to be completed in about one year.

C.—SYNOPSIS OF PREVIOUS INVESTIGATIONS.

Nearly every epoch in the medical history of this country has advanced *one factor* as being concerned in the etiology of this disease. Until

recently various physical phenomena, as well as fruits, air, water, soil, and especially miasms, have been considered as being concerned in its etiology. On the advent of bacteriology much was hoped for, with the following results:

Friere, in 1883, announced the *Cryptococcus xanthogenicus* as the specific agent of the disease, having encountered the organism in the brain, muscles, liver, spleen, kidney, lungs, blood, urine, bile, vomit, and cerebro-spinal fluid. Carmona, of Mexico, in 1885, encountered an organism in the urine of yellow-fever cases at Vera Cruz, with which he associated the etiology of the disease. Gibier, in Habana, in 1887-88, isolated a liquefying organism from the intestinal canal from post-mortems of yellow-fever cadavers, and believed it was connected with the etiology of the disease. Sternberg, in 1889, isolated the bacillus X in about 50 per cent of yellow-fever autopsies. Sanarelli, at Montevideo, in 1897, isolated the bacillus icteroides in about 50 per cent of the cases studied, and for several years it was generally regarded as the specific agent. Wasdin and Geddings, in Habana, in 1900, while investigating the claims of Sanarelli, found the organism in the blood during life and at autopsies in 13 out of 14 cases.

Dr. Carlos Finlay, of Habana, in 1881, advanced the theory of the propagation of the disease by the mosquito, believing at that time that the specific agent of the disease was mechanically transmitted by the proboscis. Later, in 1887, he modified this, having isolated from the body of the mosquito an organism to which he gave the name of *Micrococcus Tetragenus febris flavis*. In 1889 he further modified his theory with what was known as Texas fever, claiming that the mosquito could be infected by feeding upon the discharges of the patient and the disease could be transmitted to the next generation. Finlay, from time to time, has made additional claims in support of his theory, but they were not taken seriously until malaria and its propagation by the various species of *Anopheles* was a well-determined fact.

To the medical board of the U. S. Army, composed of Reed, Carroll, Lazear, and Agramonte, is due the credit of furnishing the scientific proof of the theory advanced by Finlay. In a preliminary report, submitted in 1900, they state that they succeeded in producing a severe and a well-marked case of yellow fever by mosquitoes, which, from two to twelve days previously, had bitten cases of yellow fever on the first and second days of the disease. Before the Pan-American Medical Congress in Habana, in February, 1901, a second report was submitted by Major Reed, in which the preliminary report was confirmed by additional cases and data on the conveyance of the disease by this insect. The conclusions of the board were as follows:

1. The mosquito, *C. fasciatus*, serves as the intermediate host for the parasite of yellow fever.
2. Yellow fever is transmitted to the nonimmune individual by the bite of the mosquito that has previously fed on the blood of those sick with this disease.

3. An interval of about thirteen days or more after contamination appears to be necessary before the mosquito is capable of conveying the infection.
4. The bite of the mosquito at an earlier period after contamination does not appear to confer any immunity against a subsequent attack.
5. Yellow fever can also be experimentally produced by subcutaneous injection of blood taken from the general circulation during the first and second days of this disease.
6. An attack of yellow fever produced by the bite of the mosquito confers immunity against the subsequent injection of the blood of an individual suffering from the nonexperimental form of this disease.
7. The period of incubation in 13 cases of experimental yellow fever has varied from forty-one hours to five days and seventeen hours.
8. Yellow fever is not conveyed by fomites, and hence disinfection of articles of clothing, bedding, or merchandise, supposedly contaminated by contact with those sick of this disease, is unnecessary.
9. A house may be said to be infected with yellow fever only when there are present within its walls contaminated mosquitoes capable of conveying the parasite of this disease.
10. The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects.
11. While the mode of propagation of yellow fever has now been definitely determined, the specific cause of this disease remains to be discovered.

In July, 1901, an additional report was submitted by Reed and Carroll, in which it was shown that yellow fever could be transmitted by the direct inoculation of blood from a case of yellow fever to a non-immune individual. They also made a series of investigations which tended to prove that the whole blood was not necessary to produce the disease, but by first using serum and later using serum diluted with normal salt solution and filtered through a Berkefeld filter the infectious principle would also be transferred and cause the disease as readily as with the whole blood.

3. EXAMINATION OF THE BLOOD AT VERA CRUZ.

A.—EXAMINATION OF FRESH BLOOD.

A review of the literature of recent years shows that changes in red blood cells in yellow fever can not be expected. The older writers mention various disintegrations in the corpuscles that probably resulted from the poor technique of their period.

The procurement of blood specimens for examination should be done with the most rigid cleanliness, both as to the slides and cover glasses and patient, at the point selected to procure the blood. It has been our custom to use new slides and cover glasses, recently cleaned in a mixture of nitric acid and alcohol and kept in alcohol until used.

To procure dry films for staining, slides warmed to a temperature of about 40 degrees C. were brought in contact with a small drop of blood as it flowed from the wound and evenly spread in a single layer by a glass-rod spreader.

Red blood cells.—Red blood cells from a case of yellow fever, freshly spread and immediately examined, presented no visible variation from the cells of a normal individual. The size and form of the cell are normal; a few more shadow corpuscles are seen than are observed in normal individuals in temperate climates, but this was noted generally in nearly all healthy subjects living in the Tropics. No pigment could be observed within these corpuscles. The staining reactions were those ordinarily observed in health. A number of counts were made in order to observe whether there was any destruction of red blood cells at the beginning of the disease and as it progressed. In cases where the count was made on the first or second day, and then in the later days, a progressive increase in the number of red blood cells was noted from an average 4,600,000 to as many as 6,000,000. It is believed, however, that this increase is relative, being due to dissipation of fluids. In experimental case No. 1, where the count was made before and during the progress of the disease, their increase is noted.

Hæmoglobin.—A number of estimations were made with the Dare's hæmoglobinometer, at the bedside of the patient, and with this instrument a percentage of hæmoglobin proportionate to the number of red blood cells was observed in nearly every instance. In the later days of the disease the increase in the hæmoglobin was proportionate to the increase of the red blood cells. The average percentage of hæmoglobin in healthy individuals in the Tropics is about 80 per cent.

White blood cells.—As far as we could ascertain, there was no variation from the normal white blood cell in structure, pigment, vacuoles, or fat. There was, however, a marked variation in the granulation caused by the complete or almost complete disappearance of the eosinophile cell. This is due to the rapid and almost complete destruction of the hepatic cell, whereby the glycogenic function is seriously interfered with. It has been our experience that the percentage of eosinophiles, when present, was more or less proportionate to the destruction of the liver cells, with consequent variation from normal in rare instances to complete disappearance in the majority of cases. No pigmentation is seen in white blood cells in typical cases of yellow fever.

A differential count was made in a number of instances from typical cases, without presenting more than a normal variation. The white blood cell from a case of yellow fever reacts the same to stains as a normal white blood cell. The cells containing neutrophilic granules seem more conspicuous, probably on account of lack of variation with basophiles and eosinophiles, the latter being absent and the former not reacting to the polychrome stain used.

Blood platelets.—It is to be regretted that there has been little advance in our knowledge of these blood elements since the original descriptions of Bizzozero and Hayem. In the last few years staining methods have been devised which reveal structure within these bodies

hitherto undescribed. Our examination of the blood of yellow-fever cases has shown these bodies possessing properties which we have only recently demonstrated in normal blood.

While examining our fresh blood spreads from these cases, the described blood platelet was seen with its irregular borders lying free and singly in the plasma or in aggregations of from four to ten or more in irregular clumps and apparently attached to one of the glasses. In a short time, from fifteen to thirty minutes in that climate, the platelet began to lose its irregular outline, became larger, round, and more distinct by increasing its refractility, and then to establish within itself a granulation of its protoplasm, which assumes a rapid dancing motion to and fro across the corpuscle. These motile granules within the cell are due to a substance having a high index of refraction, thus shutting off the speck of light when in the proper focus. The number of these granules vary from four to twenty, depending on the size and changes in the platelet, as yet unknown.

The platelets arranged singly go through the cycle more rapidly than those grouped in clusters, though these eventually present the same changes.

Some slides were watched under the microscope to see how long these granulations continued in motion. There is but little change at the end of twenty-four hours, but without using warm stages we found the motion to cease in forty-eight hours, though there was no disintegration of the cell.

The size of these platelets vary considerably from 1 to 8 micra. All sizes can be easily distinguished by features more or less common throughout the various sizes. The granules in those of small size are consequently very difficult to see.

The presence of a body in yellow fever presenting more or less the general features of some of the *sporozoa* was suggestive enough to make comparative studies in normal subjects, as well as those suffering from the kindred disease, malaria.

In normal subjects, immune and nonimmune, living within the Tropics it was seen that this same change was effected, though more slowly, under the same conditions as in the examination of yellow-fever blood. In the examination of malaria it was discovered to be almost impossible to find them. This, however, corresponds to the known clinical data of that disease, the platelets being considerably diminished in numbers. Some of the platelets when seen undergo the same modification with the formation of granules as in yellow fever and in normal residents in the Tropics.

Staining methods were applied to bring out, if possible, the finer structure of these bodies. All combinations were used, but only those modified after Romanowsky give the desired results. In a specimen of yellow-fever blood in our possession that was promptly fixed and

stained with a modification of Romanowsky's method these bodies were seen with their irregular outlines. The protoplasm stained a faint blue; their contents shows what appears to be the granules stained, a deep eosin pink in sharp contrast to the protoplasm. The number of these granules could be estimated with more or less accuracy in this preparation; the number, we may say, is from four to twenty. In a severe malignant quotidian malarial infection, this same staining peculiarity was noted, though, as stated above, the platelets were greatly diminished in numbers.

While we had made many blood examinations, it was not our experience to observe platelets undergoing these changes in normal blood, or in the blood of other diseases, prior to this time. As soon as we returned to the States a series of studies was undertaken, and it was soon seen that under similar conditions of light and heat the same granular condition of the blood platelet is affected in normal blood at the expiration of one hour as we had observed taking place almost immediately in the blood of yellow-fever cases. Staining reactions were applied, using the same technique as that employed in Vera Cruz, with the following results:

First. In which the platelet stained a pale blue at the edges, with a well-defined though diffuse purple area in the center.

Second. In which the platelet partook of the type found in yellow-fever cases and in about the same proportion.

It is not known what influence makes this stain variable, whether it is due to the stain, its method of application, or whether there are two distinct types of platelets.

Plasma.—The plasma was examined, both in the fresh state and in the dried film, after appropriate straining. Every technique known to us was used, but the results were negative. In these examinations many structures of various shape were observed from time to time that we were not familiar with, but they were not encountered with sufficient regularity to study in detail.

B. BACTERIOLOGIC EXAMINATION OF THE BLOOD DURING LIFE.

Technique.—Specimens of blood were taken from two localities, the ear, and the median basilic vein, at the bend of the elbow, in each instance after surgical cleanliness. The skin of the ear was pricked with a sterile needle, the blood collected in sterile pipettes and immediately planted. From the median basilic vein the blood was withdrawn by means of a sterile hypodermic syringe and immediately planted. Ordinary bouillon was used as media in quantities from 10 to 100 c. c., using as a rule 2, 5, 10, and 30 drops of blood in the various flasks. Virulent cases were selected from time to time and a series of tubes and flasks inoculated. In selecting these cases particular attention was paid in getting otherwise well-formed and healthy young

adults from the first to the last day of the disease. In all of these so selected the results were uniformly "no growth."

In the first case, that of an old man then in the agonic period, an organism belonging to the colon group was isolated. This organism gave gas production with glucose, negative with lactose; produced acid, but did not coagulate milk (the milk was of very poor quality), and gave a pronounced indol reaction. This was the only organism isolated from the blood during life, and as the subject was old and practically disorganized from age and disease, the organism, outside of its presence, had no significant bearing on the disease.

It has been the general experience of investigators that vegetable organisms are not demonstrative in blood smears of yellow fever cases. We concur in that opinion.

C.—SERUM AGGLUTINATION WITH THE *B. ICTEROIDES*, *B. TYPHOSUS*, *B. DYSENTERIÆ*, AND *B. COLI COMMUNIS*.

In order to test the agglutinative power of yellow fever serum, four organisms were selected from the stock of the Hygienic Laboratory. These organisms were the *B. icteroides*, of Sanarelli; *B. typhosus*, *B. dysenteriae*, Shiga, and the *B. coli communis*. All of these organisms had reacted typically to their species.

Two methods of applying the reaction were used in each case: (1) After the method of Widal; (2) after the sedimentation test in small test tubes. All four organisms were applied to each of ten typical cases, in dilutions of 1-40, and in every instance the result was negative, both under the microscope and in the test tube.

These observations are in accord with other recent data on the specific power of yellow fever serum in its relation to the group of cocco bacilli.

4. BACTERIOLOGIC EXAMINATION OF ORGANS AT NECROPSY.

This subject was not gone into in detail more than to convince ourselves that with ordinary working media, inoculations from the spleen, liver, kidneys, and heart's blood of virulent uncomplicated cases, no organism is encountered with sufficient regularity to suggest a fulfillment of Koch's postulates. At every autopsy where cultures were taken we satisfied ourselves that death had taken place within one hour. Inoculations were made into bouillon and on agar slants, and every uncomplicated case gave uniformly "no growth." In one case with marked hemorrhagic infiltration of the lungs a diplococcus that retained the stain after Gram's method was encountered in the blood and organs, with the exception of the kidneys.

In a mosquito killed three days after having fed on this patient an examination of the contents of the stomach showed it to be filled with

partially digested blood in which a large number of these same diplococci were present. In the case from which we isolated a colon organism before death the same organism was isolated after death from the blood and organs.

To summarize, our experience was that in typical uncomplicated cases in young adults, the autopsy being performed immediately after death, the blood and organs were found to be free from vegetable organisms.

We therefore ceased our examinations of the blood and organs and turned our attention to the *Stegomyia fasciata* and a more complex series of organisms, the *protozoa*.

5. THE *STEGOMYIA FASCIATA* (FABRICIUS).

Stegomyia fasciata (figs. 1 and 2).—This mosquito was first described in 1805 by Fabricius under the name *Culex fasciatus*. Since then it has been given no less than seventeen different specific names under the same genus, the more common being *Culex teniatus* and *Culex mosquito*. Theobald in his recent monograph has transferred this insect to his new genus *Stegomyia*, under the name *Stegomyia fasciata*. As there is no better description than that given by Theobald, he will be quoted verbatim:

Female.—Head densely clothed with broad, flat scales, black and gray on each side, a white patch in the middle, in front, extending back to the neck, a white patch on each side, a thin white border to the eyes; the scales at the back of the crown with an ochraceous tinge in some lights, long black bristles projecting forward; eyes black, with silvery patches in some specimens; antennæ blackish, with narrow, pale bands; basal joint black, with a patch of white scales on the inside (appearing as two small white spots with a lens); second joint sometimes pale testaceous at the base, pubescence and verticils dark brown; palpi black-scaled, the last joint with pure silvery white scales inside and on the tip, sometimes entirely white.

Thorax dark brown, covered with reddish brown, pale golden and creamy curved scales, ornamented as follows: A pure white, broad curved band on each side, curved inward about the middle of the mesonotum and continued back as a thinner pale line to the scutellum, two thin parallel pale scaled lines between, extending about halfway across the mesonotum and more or less on to the scutellum, a short white line in front between these two, a white spot on each side of the thorax in front near the neck; scutellum with a thick row of white scales and with three tufts of bristles; metanotum brown; plurae dark brown with several patches of silvery scales.

Abdomen dark-brownish black, with basal bands of white scales; first segment densely clothed with creamy scales and edged with pale hairs; sides with patches of white scales forming more or less flat triangular patches.

Legs with the femora with the bases yellowish, dark scaled toward the apex, extreme tip pure white, ventral surface partly covered with white scales; tibiae black; metatarsi with basal white bands; fore tarsi with the first joint basally white, rest black; mid tarsi the same; hind tarsi all basally white, except the last joint, which is pure white, penultimate joint mostly white with black apex; fore and mid ungues both toothed and hind without teeth.

Wings with the veins clothed with very long, narrow, brown scales and short,

median, broad, dark-brown ones; first submarginal cell longer and but slightly narrower than the second posterior cell, base of the former a little nearer the base of the wing than the latter; posterior cross vein about one and a half times to twice its length distant from the mid cross vein.

Halteres ochraceous, sometimes the knob is slightly fuscous.

Length: 3.5 to 5 mm.

Male.—Darker than the female.

Head black with white scales in front and in the middle; antennæ brown with paler brown bands, sometimes almost white, basal joint jet black with a large tuft of pure white scales, plumes brown; palpi black with four white basal bands; proboscis black; thorax marked as in the female but much darker, and the white scales clearer and more silvery.

Abdomen with the first segment with creamy scales, bases of the second to the fifth segments white, fifth to eighth with white lateral spots; these spots also occur on the front segments, but quite at the sides.

Legs as in the female. Fore claws unequal, the larger one with a short, blunt tooth, smaller one untoothed; mid ungues unequal, untoothed; hind equal, untoothed.

Length: 3 to 4.5 mm. (Theobald.)

Habitat.—This mosquito is widely distributed, probably more so than any other species, being found throughout the tropical world and well up into the temperate zone. At one time it was supposed to be a coast mosquito, but now it is found to have spread along the commercial lines of communication to cities in the interior that furnish receptacles for breeding places. Its acclimation to the altitudes is gradual, as may be illustrated by the following example:

About twenty-eight years ago a railroad was constructed connecting Vera Cruz with the City of Mexico. Some years later a competing line was built between these cities, but going through a different part of the country. Along the line of the Mexican Railroad yellow fever was unknown in the interior. During the construction of the railroad the disease prevailed among the employees until the road reached the foothills; it then disappeared. About nine years ago yellow fever appeared in Cordoba at about an altitude of 3,000 feet, and has since been epidemic. Three years ago yellow fever appeared at Orizaba and this year (1902) there was a severe epidemic in that city. Since the construction of the railroad many cases of the disease had been received during sickness and convalescence, and many cases have developed among strangers going through Vera Cruz to that city without the disease in any way affecting the general health of the community, until three years ago.

In the second instance, along the line of the Interoceanic Railroad we know by actual observation that the *Stegomyia fasciata* has been ascending from station to station until it has now reached Carasal at an altitude of about 3,000 feet. Synchronously with the ascent of this mosquito yellow fever became epidemic in those places. El Palmar, the next station above Carasal, about 8 miles distant, does not harbor any of these insects at the present time, and though some cases were sent there from the latter station this last year, there was no

spread of the infection. Jalapa, a city of about 35,000 inhabitants, at an altitude of about 4,500 feet and about 20 miles above Carasal, does not harbor the *Stegomyia fasciata*, and though cases have been sent to that place for years from Vera Cruz and intermediate stations, there has never been any spread of the disease.

It will be seen in these instances that the ascent of yellow fever and the advent of the *Stegomyia fasciata* have gone hand in hand until they have now reached an altitude of 4,200 feet in the first instance and 3,000 feet in the second. This is the first authentic record we have of yellow fever reaching such an altitude and is another proof that, the proper conditions supplied, the disease and the insect can be introduced and cause the same destruction of life as in more tropical regions. The distribution of this insect in our own Southern States has already been dwelt upon.

In regard to the spread by ships, our observations were limited. They were only found breeding in one schooner, which subsequently went to Ship Island quarantine, badly infested with the insect. Two more instances are reported by Passed Assistant Surgeon Grubbs at the same station where the adult insect traveled on wooden vessels in numbers from the same place. In an examination of a number of iron ships this insect in its larval stage was not encountered, but it was found in the adult stage in numbers depending upon the proximity of the ship to the breeding places. Giles reports an instance where he has known this mosquito to make a voyage from Kurachi to Suez, speaking as though the transference had been made in an iron vessel. We believe such transfer by iron vessels is rare and could only be accounted for by the insects prevailing in immense numbers and the ships lying almost in touch with the residence part of the port. In the transfer by sailing vessels the conditions are different, as on these ships there is always water conveniently stored on some part of the deck suitable for breeding places, and two or three females will in a short time, through their progeny, infest the vessel. The development of the larvæ and pupæ seems to be certainly prevented aboard ships at sea by the constant agitation of the water in the containers.

Time of flight.—We may say that the flight of this mosquito is restricted to the hours of sunshine. It was taken by us occasionally, in a well lighted room as late as 9 p. m.; generally speaking, however, the period of greatest flight is in the early morning and late in the afternoon. While we speak of the flight as during the daylight, it is, of course, relative and applies only as a generality. There are instances where the insects may be encountered at other times, but not in sufficient numbers to say that it is a habit of the species. If the presence of several hundred of this species in a jar in captivity is an indication of their natural habits, it can be said that the time of flight is limited to the daylight, for when night approaches the activity of

the insect ceases, while during the daytime they are exceedingly active.

The approach to attack of *Stegomyia* is extremely insidious, usually approaching an individual on the shady side and without warning. The pertinacity of this mosquito in returning to its victim after it has been repeatedly driven off is almost characteristic. It has been noted repeatedly by us that females escaping while being transferred from one jar to another would almost unfailingly return after a few minutes and attempt to secure food from one of us. On one occasion a marked female was driven off five times during one forenoon; once she remained away nearly an hour, when her intended victim becoming tired of further timekeeping, finally recaptured her. Having satisfied its desire for food it gives vent to a triumphant note and goes in search of a resting place. It is generally agreed that an albuminous diet is essential for the maturation of the ova. The time between the acquisition of food and the complete maturation of the ova may be said to be from three to six days. At the end of this time the instincts of the insect are for ovipositing, but being prevented she seeks more food and lives on indefinitely until this act occurs. As will be referred to later on, it has been noted by us that the ova of mosquitoes contaminated by biting a case of yellow fever undergo degeneration, which probably accounts for the extended life of contaminated mosquitoes of this species.

Aside from the daily variation in the flight of this insect, there are seasonal prevalences which must necessarily vary with the temperature and rainfall of any particular locality. The flight of *Stegomyia* is in Vera Cruz an almost uninterrupted one throughout the year. On our arrival in the city in the early part of May it was very numerous; in fact, there was no appreciable increase throughout the subsequent two or three months. In July, however, frequent rains kept flushing the barrels, washing out a great many larvæ and pupæ, which apparently perished. The decrease of *Stegomyia* at this time was noticeable; with it also came quite a reduction in the number of yellow fever cases. From the statistics of yellow fever in Vera Cruz it is evident that the disease almost disappears in some years during December, January, and February, which, no doubt, must be attributed to the fact that even in that climate the species is forced to retire from full activity for some time. With the reduction of the disease transmitters there is implied and was actually noted in July and August a decrease in the number of cases of yellow fever.

We must recall the fact, however, that most diseases at the beginning and subsidence of epidemics are usually milder than during the height of the epidemic, so that we are inclined to believe that in the colder months, while there is an actual reduction in the number of cases, there is also a great decrease in the severity of the symptoms, so that

probably many cases are not recognized. Again, like all other insects, *Stegomyia fasciata* is often more common one year than another, a circumstance which is possibly explained by the fact that they, like certain low organisms, require a period of rest; in other words, after enjoying one or two or even three or four years of full flight, the reproduction of the species becomes diminished, which for recuperation may require an equal period.

The character of the breeding places has been sufficiently dwelt upon. Any uncovered receptacle suffices for this purpose. The eggs (fig. 3) are deposited regularly, after the manner of the genus *Anopheles*, and may vary from 40 to 150 in number in a single brood. The eggs are small, about 0.75 mm. in length to 0.04 mm. in breadth. They are black in color, and are enveloped by a thin transparent membrane, which under a magnifying glass gives them a silvery appearance. In shape they are elongate, a little flatter on the upper than on the lower surface, upon which they float on the water like a miniature boat. The young larvæ hatch by dehiscence of the broader end in from ten to twenty-four hours.

Larval stage (fig. 4).—The young larvæ escaping from the eggs commence now an existence which in activity and voraciousness is scarcely attained in any other mosquito known to us at present. They never seem to rest, nor are they content to await their food like other species. They scour the water in every direction, and many times we have wondered why these larvæ seem to be larger and stronger the cleaner and freer from microscopic growth the can or barrel would be. The larvæ of *Stegomyia fasciata* are readily identified from those of other species by the shape of the respiratory siphon, which is black and barrel shaped and much shorter than in the *Culex pungens* or others. The color of the body also is different; for while the general color effect of *Culex* larvæ is usually grayish-brown, the larvæ of *Stegomyia* are whitish-gray and when nearing maturity almost milk white. In order to determine the identity of the larvæ it is necessary to dip them out of the water with a glass, when the difference in the siphon and the color may be seen at a glance.

The larvæ are full grown in from eight to ten days and then change into dark-brown pupæ (fig. 5). The identification of the pupæ is somewhat more difficult than that of the larvæ. Nevertheless, after a little experience a glance suffices to determine the pupæ of *Stegomyia fasciata* from those of other mosquitoes, and especially from those which may be found in the same water with them. The chief characteristic is the narrower and more graceful thoracic portion, which in the *Culex* species is comparatively clumsy in appearance. The respiratory siphon of the pupæ being slightly posterior to that of *Culex*, the body assumes a position horizontal with the surface of the water, with less curvature of the tail than has the genus *Culex*. The color of the

pupæ is much darker brown in *Stegomyia*; but, after all, the identification of that mosquito is just as well made from the larvæ, for they will be found at the same time with the pupæ. The complete imago escapes from the pupa case in from one to two days. The entire metamorphosis is shorter in *Stegomyia* by two to three days than in *Culex* and is completed in from eight to ten days. The difference of time in each species, of course, depends upon the temperature and supply of food.

In their characteristic breeding places the larvæ and pupæ have one trait that is of interest in connection with their destruction. When the barrel or other container with thousands of larvæ is approached and slightly agitated, the insects disappear rapidly to the very bottom, so that nearly all the water can be dipped from the barrel without removing more than a few of the larvæ. The barrel may be turned upon its side, and it will be found that about 80 per cent of the larvæ will stay in the few remaining ounces of water. In view of the fact that the greater percentage of larvæ and pupæ remained after the emptying of the barrel, it was recommended that nearly all the water be poured off and the remainder kerosened, or that the barrel be washed repeatedly to free it from larvæ. It is worthy of note that pouring water containing the larvæ of *Stegomyia fasciata* on the ground is usually as rapidly fatal to them as though they had been kerosened.

A BRIEF DESCRIPTION OF THE ANATOMY AND HISTOLOGY OF THE ADULT STEGOMYIA FASCIATA.

No attempt will be made to give a detailed description of the anatomy of the insect. Only those structures or organs that bear directly upon the investigation will be described.

The histology of the salivary glands.—Each salivary gland consists of six tubules, three in each lateral half (fig. 6). The tubules of each half of the gland unite to form the right and left salivary ducts, which soon unite with each other to form the common median salivary duct, which empties into the buccal bulb. Each tubule of the salivary gland consists of a single layer of polyhedral or short columnar cells with a large, long, central acinus. The nuclei lie usually toward the basement membrane. The central tubule of each lateral half is straight, while the remaining two, one above, the other below, are more or less convoluted, especially toward the free extremity (fig. 7). The cells of the *Stegomyia fasciata* glands in uncontaminated mosquitoes are uniformly clear, almost vesicular, thus differing from the granular type frequently met with in uncontaminated species of *Anopheles*.

The ducts of the salivary glands are reenforced with an annular arrangement of the chitin somewhat like the spiral arrangement in the tracheæ. The lining membrane consists of a single layer of epithelial

cells attached to a basement membrane; the nuclei of the cells lie close to the basement membrane.

The alimentary canal is divided into a fore-gut, mid-gut, and hind-gut, with the following subdivisions:

Fore-gut.....	{ Mouth. Pharynx with pumping organ. Esophagus. Esophageal diverticulum.
Mid-gut	{ The homologue of the proventriculus. The stomach. The pylorus.
Hind-gut	{ The pyloric dilatation. The small intestine. The colon. The rectum.

Fore-gut.—The mouth and pharynx are lined with chitin; the esophagus and esophageal diverticulum consist of a thin membrane composed of flat cells, extending from the pumping organ to the proventriculus above and down into the abdominal cavity ventrally (the diverticulum) (fig. 8).

Mid-gut.—The mid-gut extends from the proventriculus to the origin of the Malpighian tubules (fig. 9). The anterior portion of the midgut is narrow, the posterior dilated. Both are lined with a single layer of short columnar cells with nuclei almost in contact with the basement membrane (fig. 10).

The pylorus approaches a true valve structure by an apparent invagination of the epithelium into the stomach.

Hind-gut.—This part of the intestine is lined throughout with short columnar cells with large nuclei. In the pyloric dilatation the five Malpighian tubules enter. The small intestine presents a series of convolutions, dilates to form the colon, and later to form the rectum. In the rectum are seen six papillæ, the rectal glands (figs. 11–12).

The reproductive system.—This system consists of the—

1. Ovaries.
2. Oviducts.
3. Mucous glands.
4. Spermatheca and ducts.

In the young adult female mosquito the ovaries are attached to the fourth and fifth abdominal segments. As they become mature after fertilization and an albuminous diet they gradually occupy the whole of the posterior abdominal segments (fig. 13).

The balance of the reproductive system is not of interest in connection with this investigation.

The muscle plates of the thorax consist of faintly striated muscle cells with nuclei immediately beneath the sarcolemma arranged in rows (fig. 14).

6. THE CONTAMINATED *STEGOMYIA FASCIATA* AND ITS PARASITE

In order to secure contaminated mosquitoes for examination, about twenty large young females should be selected from the breeding jars and placed in a specially prepared cage, made with three sides of wire gauze and one side of glass for observation. A cheese-cloth sleeve at the top makes the mosquitoes accessible and permits the patient to place his hand inside the cage.

After the mosquitoes are placed in the cage it is set aside for several hours, so that they will become hungry. The cage is then taken to the bedside of the patient, his hand introduced and permitted to remain therein until the mosquitoes have gorged themselves with blood. The time required for this is variable. As a rule it may be stated that all that are going to feed will do so within thirty minutes. The cage is then taken to the laboratory and placed in a subdued light for twenty-four to thirty-six hours without the addition of food of any kind. At the end of this time it will be found that all of the mosquitoes that did not feed have died.

A few male insects should be added to the cage and artificial feeding begun. Three articles may be used as food: (1) The blood of those sick with the disease, (2) bananas or other overripe fruit, and (3) cotton well moistened with a thin sirup. The first and second answer best, with preference for the first.

With this technique mosquitoes can be kept alive for several weeks.

Previous to killing they should not be fed for one or two days, as the stomach will be found so thin by distension that satisfactory examination is impossible.

From almost every case studied in detail a large number of insects were contaminated and their killing commenced on the second day and continued at stated intervals until between the twentieth and thirtieth day. After killing they were embedded in paraffin, cut serially, and appropriately stained. While contaminations were made from cases of yellow fever as late as the seventh day of the disease, most of our attention was given and practically all our results were obtained from mosquitoes contaminated during the second, third, and fourth days. The results of the examination of mosquitoes contaminated on different cases were fairly uniform, a large proportion of the insects presenting one or more stages of development of a well-defined animal parasite.

Sections of mosquitoes killed two or three days after contamination showed the stomach distended with undigested blood. In this no organism could be demonstrated to our satisfaction. With the disappearance of the blood on the third day after feeding by the process of digestion a parasite became plainly visible and could be traced through the following stages with more or less accuracy.

Beginning, then, with three or four day mosquitoes, after the disap-

pearance of the blood, we observe in the stomach cavity varying numbers of small fusiform-shaped protozoa (fig. 15), lying principally in groups, though many are single. These fusiform-shaped bodies are well defined, with an oval central nucleus. In studying the groups we noted certain bodies which bear a striking resemblance to cases of terminal conjugation such as are described for certain sporozoa. While these conjugating bodies are noted principally in the stomach cavity, they are not necessarily confined to that organ; we find in two specimens having a large number of such bodies that they have passed through the stomach wall and are undergoing the same apparent conjugation in the esophageal diverticulum where subsequent changes take place.

The stomach wall has undergone some modification during this process. It has become hypertrophied and shows many bodies similar in shape to those found in the localities mentioned, but naturally can not be so readily identified as when lying free. However, as they are found only in the stomach and diverticulum we know of nothing that could cause us to err if we say they are the same. We may say, then, that after this apparent conjugation the resulting body (zygote) passes through the stomach wall into the esophageal diverticulum. We then find in the diverticulum (preserved specimens in microtome sections) a mass of material the nature of which is at present not entirely clear to us. It has more or less the appearance of an albuminoid mass, but its origin and exact nature still remains to be explained. In this mass, more particularly at the periphery, we observe further developmental stages of the parasite; the latter has increased in size, its nucleus has undergone fragmentation or multiple division (fig. 16). The resulting chromatophilic granules from this division now rapidly increase in size, become rather sharply defined and more or less regularly elongate oval, the "sporoblasts?" (figs. 17 to 24).

The "sporoblasts?" are more or less definitely limited in the early stages by a membrane. Later this becomes so thin as to be imperceptible, though the aggregations of "sporoblasts?" still retain their well-defined areas until the disintegration of the encysting albuminoid mass in which the development takes place. The number of "sporoblasts?" in each "oöcyst?" is rather constant, thirty or forty being visible in each median section. As the albuminoid mass disintegrates and the "sporoblasts?" become mature the latter are liberated (figs. 25-26).

In order to appreciate the phases that are to follow, the anatomy of the esophageal diverticulum must be clearly comprehended. A reference to figs. 8, 9, and 11 will show the relations of the diverticulum. Beginning at the homologue of the proventriculus, the diverticulum passes downward in contact with the anterior constricted part of the midgut. Here it is surrounded by the six tubules of the salivary gland, three on each side, and in contact with it through the intervention of a delicate reticulum of connective tissue.

The position of the posterior or dilated portion of the midgut (the so-called stomach) depends upon the state of distention of the diverticulum, it being in contact with that structure superiorly (dorsad) as far down as the pyloric dilatation and inferiorly (ventrad) with the connective tissue of the abdominal segments, so that a protozoan parasite passing through the midgut in the direction of least resistance (ventrally) enters this diverticulum and undergoes future stages of development. In malaria the sporozoite formation is said to take place in the stomach wall of the mosquito, but this we believe to be an error in interpretation, the significance of this diverticulum, its unobstructed connection with the thorax, and intimate relations with the salivary glands not being thoroughly appreciated.

After the liberation of the "sporoblasts?" migration commences in the direction of least resistance, which is, as stated above, toward the thorax. Arriving at the anterior (cephalad) part of the diverticulum they are, with the exception of that thin structure, in contact with the salivary glands on all sides except above (dorsad), the upper border being occupied by the anterior constricted part of the midgut. The "sporoblasts?" then penetrate the diverticulum and become disseminated throughout the connective tissue supporting the gland (figs. 27, 28). The "sporoblasts?" then enter the gland structure and gain access to the salivary cells, where another important phase takes place. This phase consists in the breaking up of the resting "sporoblasts?" (which now apparently become the spores) into a number of infinitesimally small "sporozoites?" (figs., 29, 30), which ultimately are freed, find their way into the lumen of the gland, and would naturally be discharged by the insect in the act of procuring food.

We have now followed and illustrated four important and pronounced stages of an animal parasite which we have encountered in mosquitoes fed on cases 11, 21, 36, and in some scattering cases studied before the organism appealed to us as probably being connected with the etiology of yellow fever. We have produced yellow fever experimentally with mosquitoes from case 36 that harbored this parasite and have again found the parasite in mosquitoes fed on this case.

As further evidence we permitted this same species of mosquito, *Stegomyia fasciata*, to feed on a case of malarial fever of the malignant quotidian type, on normal blood, and on sugar and water. *In none of these mosquitoes did we find the parasite described above.*

Systemic position.—From the description given above it is clear that we are dealing with a sporozoön which in all probability is passing through its sporogenetic (sexual) cycle. The stages found remind one very strongly of the corresponding cycle of the malarial parasite, and the inference would not be unnatural that the schizogonic (nonsexual) cycle would be similar to that of *Plasmodium*. Still, not only we, but Sternberg, Reed, Carroll, and others have made careful

studies of the blood in cases of yellow fever without finding any structure which could be legitimately interpreted as the schizogonic cycle of the parasite now under discussion. Until that cycle is found a definite systemic position of the order or family of the Vera Cruz organism is scarcely possible. We do not see how it can be legitimately united generically with any of the sporozoa thus far described, and on this account, and especially because of its probable importance in connection with yellow fever, we think the action of proposing for it a new generic name is not unwarranted. Pending further investigation we suggest that the parasite be provisionally placed in the *Hæmosporidia*, but we frankly state that this proposition is one based entirely upon practical considerations of convenience rather than upon a conviction of its exact position.

As generic name we propose—

MYXOCOCCIDIUM Parker, Beyer, Pothier. 1903.

Generic diagnosis.—Ordinal position uncertain.?? *Hæmosporidia*: *Schizogonic* stage unknown. *Sporogenic* stage: A fusiform stage 3 to 4 μ long by $1\frac{1}{2}$ to 2 μ broad, in the lumen of the stomach and esophageal diverticulum, seen about three days after mosquito has bitten yellow-fever patient; nucleus present. A globular stage (?oocyst) in the esophageal diverticulum, imbedded in an albuminoid mass of undetermined origin and nature. This reaches maturity and breaks up into numerous elongate-oval bodies (?sporoblasts) 3 μ long and 2 μ broad, which enter the cells of the salivary gland, where, coming to rest (?spores), they break up into numerous excessively minute (?sporozoites).

As specific name we propose *STEGOMYIAE*, on account of the organism being first encountered in this genus of mosquito—

MYXOCOCCIDIUM STEGOMYIAE Parker, Beyer, Pothier. 1903. (Figs. 15 to 31.)

Specific diagnosis.—*Myxococcidium*.—Same as generic diagnosis.

Habitat.—The yellow-fever mosquito, *Stegomyia fasciata*, in Vera Cruz, Mexico.

Type specimens.—In collection of the Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service.

The examination of other structures in contaminated mosquitoes.—The other organs of the mosquito present evidences of marked alteration, both in structure and function. Beginning with the ovaries of a mosquito fed on normal blood, we find the ova undergoing immediate hypertrophy, distending the whole abdominal cavity (fig. 18), pressing the other organs forward and downward. In mosquitoes contaminated by feeding on a case of yellow fever the ova primarily take on a hypertrophy, but subsequently begin to degenerate until there is practically nothing left but fibrous tissue (figs. 31, 32). We have attached considerable importance to this, believing that this degeneration alters the natural habit or instinct of the insect and prolongs its life for some time, owing to the suspension of the process of ovaposition. No parasite of any kind, however, could be demonstrated undergoing development in these ova.

The salivary glands of a normal mosquito are presented in figs. 6 and 7. They undergo considerable change in contaminated mosquitoes. There is at first a slight hypertrophy of the glands of mosquitoes fed on normal blood, but in those fed on yellow fever the glands undergo excessive hypertrophy and become convoluted, forming large masses of gland structure (figs. 33, 34) rather than the individual tubules seen in normal blood-fed insects. Outside the simple addition of the spores and sporozoites no structural changes could be noted in these organs.

7. EXPERIMENTS.

In order to have a demonstration of the transmission of yellow fever by the mosquito, to study the changes that are present in the tissues of the mosquito and to study the changes in the blood of the subject, it was decided to attempt the inoculation of an individual.

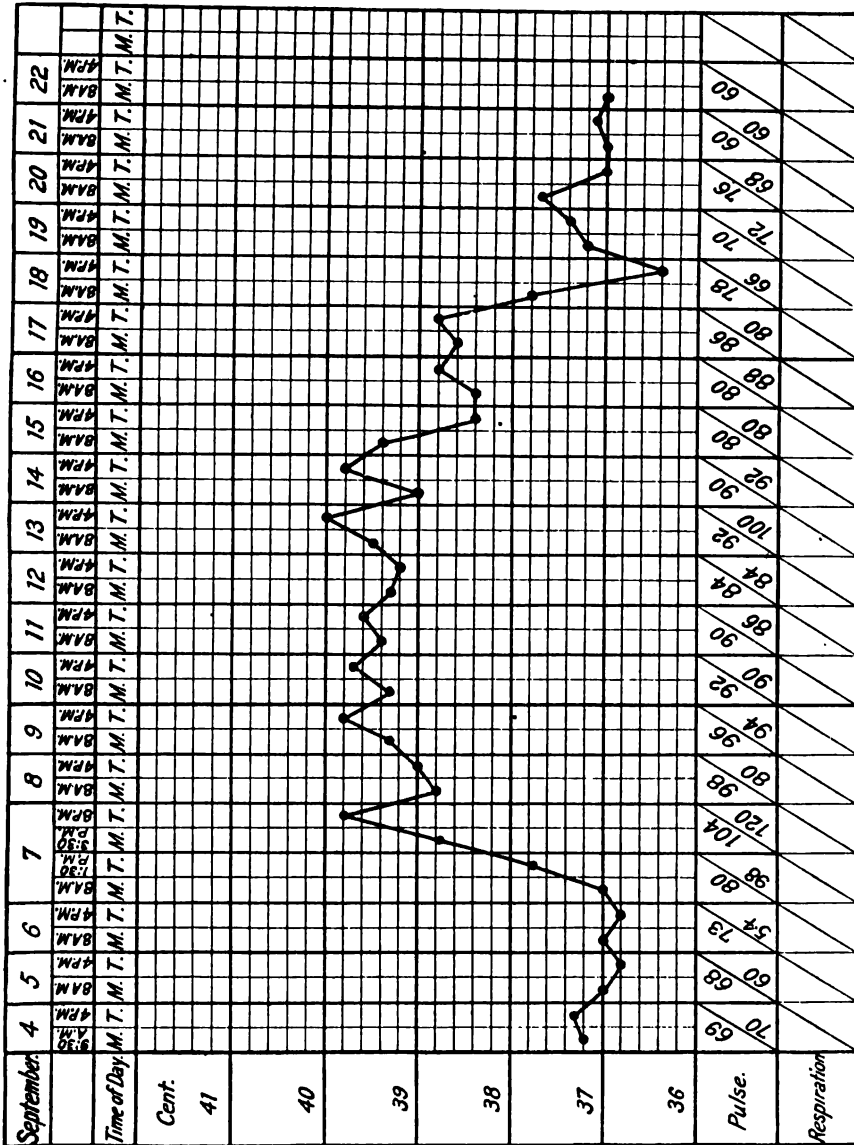
A room was made sufficiently mosquito proof and a man brought from Jalapa, a town of 4,500 feet altitude and as yet free from yellow fever.

In this work we associated with us in full confidence a commission appointed by the Mexican Government, consisting of Drs. Matienzo, del Rio, and Iglesias, all men of large clinical experience and ability, who agree to all the following statements in this case. There was also associated with us at this stage P. A. Surg. M. J. Rosenau, Director of the Hygienic Laboratory, who observed the case from September 5 to recovery, and who also agrees with the details as presented.

Experiment No. 1.—A. G., aged 26 years, native of Jalapa; had been a resident of Teocelo, a mountain village, for many years and was an ironworker by trade. He had never visited the coast. This man had been a prisoner in one of the jails for the past twenty-two months and was brought from there to Vera Cruz with his full consent and permission and placed in a mosquito-proof room for observation and experimentation. He was examined physically and found to be free from organic lesions. The urinal examination was with negative results. An examination of fresh blood was made, which showed a few shadow blood corpuscles and blood platelets; the granulations of the polynuclear neutrophile were especially marked; Müller's blood dust was present; the red blood cells were of good color and form, and free from intracorpuseular bodies. The estimation of the blood elements is as follows:

Red blood cells.....	4, 650, 000
White blood cells	6, 355
Hæmoglobin	per cent.. 80
(a) Lymphocytes.....	per cent.. 19.4
(b) Large mononuclear.....	do..... 8.8
(c) Polynuclear	do..... 67.4
(d) Eosinophiles.....	do..... 4.4
	100

The day following his arrival, September 4, at 9.30 a. m., two mosquitoes were permitted to feed on the left hand. These mosquitoes had previously been permitted to feed on a severe case of yellow fever on August 13, at 8 a. m., forty-one and one-half hours after the chill,



and had been fed on sugar and water to this date, twenty-two days and one and one-half hours. The mosquitoes were killed immediately after feeding and subsequently sectioned for histological examination.

The temperature, pulse, and general condition were taken regularly

at 8 a. m. and 4 p. m. without variation until September 7. On the afternoon of September 6 a small body slightly smaller than a red blood cell and containing four or five bodies that about filled the cell inside the membrane was discovered. These bodies moved slowly about one another, but as no more were found it did not justify further mention. On the morning of September 7 the patient awakened after a good night's sleep and had coffee and bread. At 11 a. m. breakfast was brought, but was not eaten with relish; at 11.30 a. m. a headache, especially frontal, developed, along with vague pains in the shoulders and knees. At 1.30 p. m. all pains were severe. There had been no chill, rigors, or nausea. The temperature was taken here and found to be 37.8, pulse 98. Counting from the beginning of the headache, it was seventy-four hours since the infection by the mosquito on September 4. The pulse and temperature went up rapidly. Some vomiting occurred after taking medicine in the evening and the following morning. The gums became congested, the eyes bright and suffused, and the case generally assumed the type of severe infection.

The blood was examined at this stage, but there was slight deviation from that previously reported. The character of the blood plate seemed to have undergone some modification. Instead of staining with a pale purple central zone with blue body, the central zone seemed to have broken up into highly fractile, small points, that stained beautifully with eosin and Goldhorn's methylene blue. For some time this excited considerable attention, but later it was found that normal blood of certain individuals gave reactions that closely simulated the above description.

On September 8 mosquitoes were contaminated by permitting them to feed on the hands and wrists. These mosquitoes were subsequently killed on different dates and examined histologically. It was decided to examine the blood systematically at night at two-hour intervals. On the night of September 9 fresh specimens and smears were examined. The specimens showed nothing abnormal. On September 10 an examination of the blood was made, with the following results:

Red blood cells.....	5,217,500
White blood cells	2,666

A differential count was not made, but after examining several hundred white cells the entire absence of eosinophiles was noted. The patient grew gradually weaker; the jaundice and bleeding from the gums became marked; black vomit subvened; the urine contained more and more albumin until 5½ grams per 1,000 c. c. were recorded in the Esbach albuminometer. The albumin then came down to 4 parts per 1,000 on September 19, the day that the temperature returned to normal. The next day all albumin had disappeared, but the urine contained bile pigments in considerable amounts, but gradually returned to the normal. Owing to the rather critical condition

of the patient, all further attempts at study were abandoned until his complete recovery and discharge at the end of September.

The albumin in the urine was more or less remarkable on account of its rapid disappearance at the end of the disease. Following is a tabular statement of the urine:

Date.	Cubic centimeters.	Parts albumin per 1,000.
September 12	1,200	0
13	1,200	1
14	1,000	1½
15	1,100	4
16	1,200	3½
17	800	4
18	700	5½
19	850	4
20	1,000	0

In order to make this picture complete some repetition from the chapter on the contaminated mosquito is necessary. The mosquitoes used in this experiment were examined and in the salivary glands were seen spores filled with sporozoites in various stages of maturation. The mosquitoes in the same jar that did not feed showed the presence in their salivary glands of the same bodies as described and illustrated. In the mosquitoes fed on the experimental case and subsequently sectioned and examined the conjugating bodies are plainly seen on the fifth day after contamination. The remaining stages to the sporozoite are obscure on account of the diet, sugar and water, which was used. We believe that had we continued an albuminous diet, as in cases 11, 21, and 36, all the phases in these mosquitoes would have been as clearly presented as in the illustration.

After the success of this first case it was agreed to continue the experiments on other lines. In this continuation three more individuals were used without adding anything new to our knowledge of the disease.

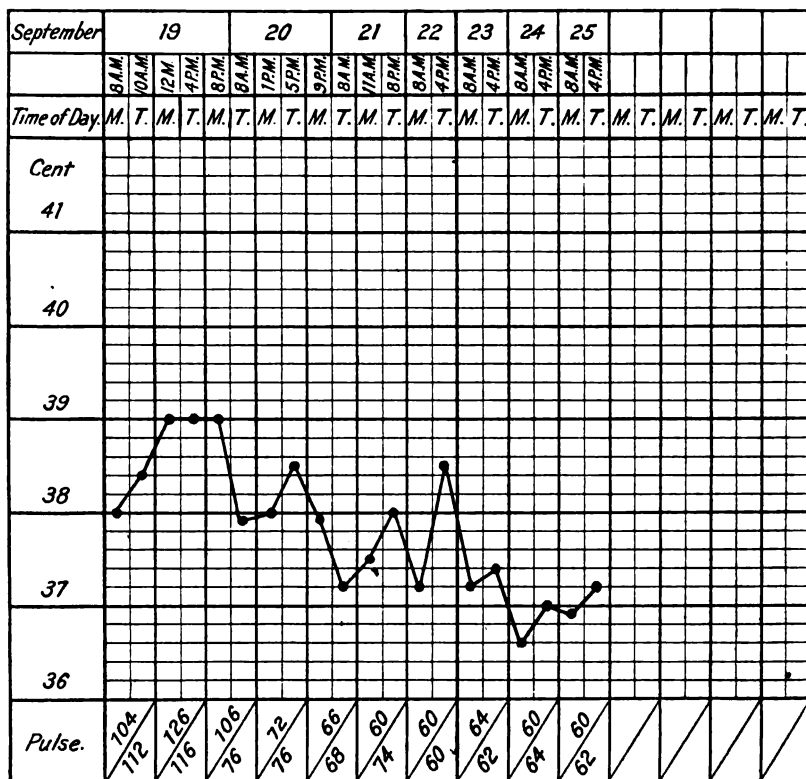
Experiment No. 2.—Benites; aged 27 years; a native of Jalapa; had lived there all his life with the exception of thirty days that had been spent at Vera Cruz some eight years ago; a shoemaker by trade; for the past nine months had been confined in one of the jails.

On September 9 at 9 p. m. this man was inoculated with blood serum from the vein of Experiment No. 1. The blood was drawn in sterile syringes and defibrinated. It was then diluted with two volumes of normal salt solution and filtered through a Berkefeld filter. 0.1 c. c. of this mixture was used for inoculation. The temperature of this man was taken every four hours for the next six days without variation from the normal. The experiment was then considered negative.

On the morning of September 19 he awakened with dull sensations in the back and legs. Shortly afterwards a headache and pain in the

knees and ankles developed. The temperature and pulse increased, and toward night a more or less typical case of yellow fever was diagnosed. This case was treated energetically from the beginning, and was mild after the first twenty-four hours. The urine was examined daily without detecting the presence of albumin. The case made a good recovery after five days of fever.

It is interesting to note that this case developed nine days twelve hours after the time of injection, and eleven days twenty-two and one-half hours from the time the first experiment was taken sick. From the history of the case that follows we agree that there must be some



loophole wherein a mosquito had gained access to the room, had become infected, and transmitted the infection to this man. It would seem more reasonable to believe this than that the period of incubation after the injection was nine days twelve hours.

Experiment No. 3.—A. C.; aged 21 years; native of San Antonio, State of Tlascala; lived in the neighborhood of Jalapa for the last nineteen years.

This man was inoculated with 1 c. c. of serum used to inoculate Experiment No. 2. Time of inoculation was 9 p. m. September 9. There was a slight febrile reaction on the following day, the tempera-

ture rising to 37.6, but returned to normal the following morning. From that time until his discharge on September 20 the man remained normal. He was transferred back to Jalapa and kept under observation several days with negative results.

Experiment No. 4.—This experiment was undertaken to discover whether infection could be conveyed by drinking water.

P. L.; native of Salaya; aged 22 years; had never been near the coast; for the last twenty-seven months had been in jail in the mountains. He arrived at Vera Cruz at noon on September 10 and was immediately placed in the mosquito-proof room. On September 11 four mosquitoes from the same lot used in Experiment No. 1 were crushed in drinking water and given the man to drink. The man was kept under observation until September 20 and then returned to the country, where he was still under observation. No reaction or deviation from the normal occurred during this period of observation.

8. SPECIES OF MOSQUITOES IN VERA CRUZ

While most of the time and study of the working party was directed to the investigation of yellow fever, some attention was given to the determination of the varieties of mosquitoes, their distribution and habits, in the city of Vera Cruz and surroundings. Upon the arrival of the working party May 12, and for some time afterwards, but few mosquitoes were encountered, but as summer advanced the number of species increased until it had reached, at the conclusion of our work, a maximum of fifteen. This list, though large, is undoubtedly not complete, for, while the city is surrounded by low and swampy country, the almost complete lack of woods of any kind explains the absence of many sylvan mosquitoes and restricts these insects in their representation to the domestic and rural varieties alone. In the early part of our sojourn only four or five species could be identified and it was not until the latter part of June that other varieties were taken. The species determined by us appeared in the following order: *Culex pungens*, *Tæniorhynchus perturbans*, *Anopheles argyrotarsis*, sub. sp. *albipes*, *Culex confirmatus*, *Culex nigripes*, *Culex stimulans*, *Culex tæniorhynchus*, *Tæniorhynchus fasciolatus*, *Janthinosoma Lutzii*, *Anopheles maculipennis*, *Anopheles pseudopunctipennis*, *Culex sollicitans*, *Punoplitès pseudotitillans*, and *Psorophora scintillans*.

Culex pungens, the first mosquito noted, is too well known to need any further description. Its life and habits are the same in Vera Cruz as elsewhere. Wherever found it is a gutter breeder, and the filthier the gutter and the more stagnant the water the greater its prolificacy. It may be stated here that owing to the daily and continual flushing of the gutters by the heavy rains this species was even less prevalent in Vera Cruz than in many other and more temperate regions. This species may be properly termed a domestic mosquito, preferring the

somewhat a surprise to us to find it so far south as Vera Cruz. Owing to the small numbers in which it was observed no particular attention was given to it.

The same remarks may also apply to *Culex confirmatus* Arribalzaga (fig. 39), for while several specimens were taken by us in the city, it can not be considered as an insect of importance or as one having any relation to hygiene. Since its original description by Arribalzaga the distribution of this insect has been found to be even greater than given by Theobald. It is found not only in the United States, but this locality has now been added to its habitat. It is a handsome insect, of medium size, conspicuous in appearance on account of the large patch of silver-white scales on the thorax. Its eggs and the manner of depositing them are somewhat similar to the *Stegomyia fasciata*.

During the month of June our laboratory was invaded nightly by a mosquito which heretofore had scarcely been regarded as a southern species, but which, according to our experience in Vera Cruz, it no doubt is. This mosquito, *Culex nigripes*, or, better, *Culex impiger*, is, wherever it does occur, a veritable nuisance. In size it is small, but a stoutly built insect. Its flight was an exceedingly short one, and was over after two or three weeks' duration.

About the middle of August one of the sanitary officers brought a number of very large larvae and pupae to the laboratory, which had been obtained by him from a small pond just outside of the city limits. In the course of two or three days the adults emerged, which, compared with the size of the larvae, were very small. In fact, we believed at first that the larvae were those of *Psorophora*. They proved to be *Taeniorhynchus fasciolatus* (fig. 40). Unfortunately, owing to the other pressing work, we failed to obtain any illustrations or measures of the larvae and pupae, which at this time are still undescribed. The single insect from which the illustration was made we secured much earlier in the season, June 25th. The insect is dark colored and large, the thorax is very dark-brown, somewhat lighter in the middle and carries on its side a patch of white scales. The abdomen is nearly black, with six silver-white spots just above the pleural membrane. The chief characteristic of this species is the pure white ring or band on the apical end of each femur. Theobald only reported this mosquito for Brazil and Argentina.

Another species of mosquitoes which we determined and which only thus far has been recorded in the lower Amazon and Rio de Janeiro is *Janthinosoma Lutzii* (fig. 41), described by Theobald as a new species. It is a large and very handsome insect adorned with brilliant metallic blue and purple scales on the abdomen and legs, and golden-yellow scales on the thorax. Its flight in the city was very short, but in the swamps outside of the city limits it was a veritable scourge. Its bite is very severe and irritating for a long time. It entered the shipping

in the harbor, as we determined by examination of the vessels in port, where among a variety of mosquitoes found in the quarters and holds *Janthinosoma Lutzii* was one of the most numerous.

Psorophora scintillans Walker (fig. 42) is another species whose range has been extended according to our observations. Theobald or rather Walker, records it only for Para. How Theobald comes to describe the insect with the proboscis curved as in *Megarhinus* it is impossible to understand. All of our specimens had a straight proboscis during life and retained it after death.

The fourteenth species, *Panoplitus pseudotitillans* Theobald (fig. 43) was noted by us at the latter part of our stay. It is a small brown and yellow, but dark looking insect and no doubt is a swamp mosquito.

The general characteristics of *Panoplitus* are in this species exceedingly well represented by the densely scaled wing veins; the scales themselves are broad and asymmetrical. In the city we did not find the insect in numbers, but they were reported to us as being exceedingly vicious in the swamps, and especially along the seashore. Since *Panoplitus* has been shown to act as the host to *Filaria Bancrofti*, some attention should be given to the life history of this mosquito. Filariasis, however, is said to be rare in or about Vera Cruz, only one reported case being known to the members of the working party. No examination of the case was made to verify the disease.

9. THE TRANSFERENCE OF MOSQUITOES BY SHIPS.

This subject was not studied in detail on account of lack of facilities, but sufficient information was gathered to make it worth mentioning. The only time we found mosquitoes actually breeding on board a vessel was in the instance of the American schooner *John H. Crandon*. This schooner had arrived from Mobile, Ala., with a cargo of lumber twenty days previous to our examination. Water and provisions had been taken on at Mobile. The examination was made on account of a case of yellow fever occurring among the crew. The wooden tanks were examined and found to contain larvae of *Stegomyia* by thousands. The iron water tanks were examined, but owing to their depth and small openings none were found. Iron water tanks, as a rule, are more securely covered and are given more attention than the wooden containers. The two or three barrels, placed in front of the galley and forecabin, are more frequently infested and in every instance preference was given them in the examination. The box of carpenter's grindstone offers another favorite place for the breeding of this insect. An examination of the cabins was made to determine the presence or absence of adult insects. In the room from which the man with yellow fever was taken, the insects were found in abundance, both normal and blood fed, resting in the shady corners on dark objects hanging around the room. Considerable effort is necessary to detect mos-

quitoes when they are few in number; each cabin should be gone over systematically, passing the hands in the corners and gently shaking the hanging articles until every object above the floor has been gently disturbed. The forecabin and galley of this schooner, immediately behind the breeding barrels, harbored the insect in abundance.

The steamship *William Cliff* is of interest in connection with the transference of mosquitoes by vessels as well as furnishing data relative to the period of incubation and spread of malaria among a crew where all outside influences were removed.

This vessel sailed from Liverpool, England, on May 29, 1902, with the following itinerary:

Arrived.	Port.	Sailed.
June 11	St. Thomas	June 12
June 15	Colon	June 16
June 19	Kingston	June 20
June 25	Tampico	June 26
June 27	Vera Cruz	July 1

Until arrival in Tampico no sickness had occurred on board; while leaving that port one man was taken sick with a vague chill, and illy defined pains. Two days later, June 28, four of the crew were taken sick with pronounced chills, pains in the head, extremities, and back, and high fever. The following day, June 29, four more including the captain, were taken sick in like manner; on June 30, two more were taken sick.

On June 29, the blood of two of the cases was examined for the plasmodium malaria with negative results. Their absence was accounted for by the large doses of quinine administered prior to the examination. On July 1, two new cases were examined; in one the tertian parasite was obtained, the other was negative.

The disease clinically was of the tertian type, about half-intermittent, the balance remittant. All, with one exception, responded readily to quinine. The exception resisted the quinine for three days. An examination of the ship was made to determine the genera and species of mosquitoes on board. Of these there were three genera and four species in abundance, as follows:

Anopheles argyrotarsis,
Culex fatigans,
Culex teniorhynchus,
Janssinosoma Lutzii.

All the varieties mentioned were found in the forecabin and after wheelhouse, the crew's quarters being aft instead of forward. The cabins failed to show the presence of mosquitoes on the examination of June 30, nor were any noted previous to that time.

Anopheles argyrotarsis were present in Vera Cruz, though in very

traction on the head with a flat needle. With a little practice, the salivary glands may be examined *in situ* by carefully approaching those structures through the dorsal tissues.

Paraffin or celloidin embedding is more complicated than the above, but possesses greater, and when cut and mounted serially, absolute accuracy.

The steps in the process may be briefly described as follows:

Killing.—Two methods were employed: First, the mosquito was taken from the jar or cage in a small test tube, stunned with tobacco smoke, and then placed in the fixative; second, instead of using tobacco smoke, the test tube was inverted over a small bottle of fixative; the mosquito soon fell into the fluid.

Fixing.—We have separately and collectively used all the fixatives used in ordinary and special histological work. There is no doubt that bichloride of mercury, osmic acid, and the salts of chromium, in their various combinations, give the same excellent results as fixatives in mosquito work as in histological work. The mosquito, however, can not be manipulated after fixation as ordinary histological specimens, on account of the liability to break certain parts of the chitin. Even with special effort to remove every trace of the fixative, a certain amount always precipitates as an oxide, which prohibits their use in this connection. Cut sections filled with or containing pigment in parts is a source of error which must be guarded against.

In order to obviate the disadvantage mentioned, absolute alcohol was selected, and proved so satisfactory that it was used throughout the work. The mosquito was permitted to fly or fall directly into the alcohol and remain there one or two hours; it was then transferred to a watch glass, the legs pulled off with forceps, the wings carefully cut near their attachments, and then transferred to another change of absolute alcohol for two hours to secure *dehydration*.

Clearing.—After the second change of absolute alcohol the insect is transferred to xylol, where it remains until clear, usually half an hour. It is then transferred to another change of xylol, and placed in the warm chamber of the paraffin bath. Here, from time to time, a few drops of liquid paraffin are added until the xylol is well saturated. It is then transferred to soft paraffin for one to two hours, then to paraffin of 52 melting point, and after one hour is ready for embedding.

Embedding.—The same general features are used in the embedding of mosquitoes as in histological work. It is better, however, to embed on small blocks of wood that have a coating of hard paraffin about 2 mm. thick on the embedding surface. This is inclosed in a paper box. The box is filled with melted paraffin, the mosquito is taken by the proboscis and quickly transferred to the box, placed in position, and then put on ice for rapid congelation. When the block is

orientated the mosquito will be found in perfectly translucent paraffin, so necessary for good serial cutting.

Orientation.—Care should be taken not to approach too closely to the mosquito, as our experience was that the chitinous structure cuts much better if supported by a generous portion of paraffin. The orientated block should be oblong, and for the serial sections that are to follow should have accurately cut parallel sides.

Sectioning.—We were unfortunate in the selection of a microtome for this most important work, having taken one of the sliding microtomes after the model of Schanze. The Minot rotary microtome is about the only model that gives good results, though the Cambridge rocking microtome is a fair substitute. Two things are essential for success in paraffin sectioning in the Tropics; the block and instrument should be chilled and the sections cut in the early morning when the temperature may be several degrees lower. The sections should be cut serially and immediately placed in cold water to permit them to flatten before mounting. The knife should be examined frequently during the sectioning, as the chitin sometimes turns the edge, thus ruining the sections that follow.

The thickness of the section is a matter of considerable importance: it depends upon the nature of the work, whether for histological study or for study of developing sporozoa. In the first instance, a uniform thickness of 20 micra is about as thin as can be depended upon; in the latter an average of 15 micra. Sections of 10 micra or less show too little structure to be of service and possess no advantage for any phase of the work.

Sagittal sections are better adapted for manipulation and examination than other sections. The anatomic planes can also be more easily followed.

Mounting.—Two or three rows of sections, each about 45 mm. in length, should be floated on a slide and the water drained off. The specimen should then be covered with rice paper, moistened with 80 per cent alcohol, and then flattened with blotting paper under careful but considerable pressure. The slides should then be set aside, and protected from dust until thoroughly dried. Unless this latter mechanical dehydration is perfect, the section is apt to wash off in the subsequent treatment. If dry, the specimen will stand the same amount of manipulation as though a mounting medium had been used.

The use of albumen, acacia, or starch fixatives is condemned as being unclean and unnecessary.

Removing the embedding material.—This is accomplished with xylol in the same manner as in histological work.

Staining.—This most important part of the work is still in its infancy. It can not be said that there is a single or combination of stains that give results that are perfectly satisfactory. We have tried at various

times hæmotoxylon, either alone or in combination with eosin, Romanowsky's with Jenner's modification, and the various preparations of methylene blue and thionin, with the same results—partial success.

The stains that gave us the best results, and with which we believe the whole future work will depend upon, were the iron hæmotoxylon, after the method of Heidenhein, and a saturated solution of Bismarck brown in hot 60 per cent alcohol. The results in either instance, when properly applied, will be a precise nuclear with a faint ground stain, or, with further differentiation, a purely nuclear stain of great brilliancy. In choosing between these two stains it should be remembered that the hæmotoxylon is specially adapted to the staining of some phases of protozoa, while the latter selects the protozoa secondary to the histology of the insect.

Dehydration.—Dehydration is secured by passing through the alcohols, and *clearing* with xylol. The specimen should be *mounted* in xylol balsam.

Cover glasses, 22 by 50 mm. should be used to prevent overlapping of sections or cover glasses, which invariably results from the use of smaller sizes.

Celloidin embedding.—This method finds much favor with English and continental observers and has some few adherents in this country. It was given a trial, but on account of our inability to do serial work was discontinued. We might say that it has less to recommend it in mosquito work than in finer histological work, where it has been generally abandoned. The following is the technique used for embedding:

1. Dehydration through alcohols.
2. Transfer mosquito from absolute alcohol to a mixture of absolute alcohol and ether, equal parts.
3. Transfer to thin celloidin for forty-eight hours.
4. Transfer to thick celloidin for forty-eight hours.
5. Transfer to paper mold on cork, filled with thick celloidin.
6. Transfer to 70 per cent alcohol for three days.
7. Cut sections with knife flooded with 70 per cent alcohol.
8. Stain.
9. Dehydrate.
10. Clear.
11. Mount.

MOSQUITO-PROOF ROOMS.

It is necessary in all infected centers to have quarters provided for the reception of yellow-fever cases. It will not be found necessary or advisable to go beyond the city limits to procure these quarters, as a room or ward can be made mosquito proof and thus save the patient the needless transportation which experience shows enhances the mortality of every epidemic.

A room may be hastily provided by taking a good quality of cheese or other cloth, having from 20 to 30 meshes to the inch, and placing

it over all windows and doors. The entrance should be further protected by double doors, sufficiently separated so that only one can be opened at a time. Permanent quarters should be protected by brass-wire screens, about 20 meshes to the inch, with a vestibule to preclude the possibility of mosquitoes entering. All drainage connections from this ward should be well trapped or covered with wire screen. It is safer, however, to do away with this source of contamination by directly disinfecting the excreta and transferring it in buckets to the sewer or incinerator.

Preparatory to occupying a room designed for the reception of patients having this communicable disease, all insects should be killed by one of the good insecticides. Too much dependence should not be placed in pyrethrum and tobacco, as experience has taught that a concentrated atmosphere is necessary to produce death, and too many loopholes are offered for escape. All cracks in the floor, narrow ledges over the windows and doors, should be examined, and the room should be carefully dusted and swept while the effects of the drug are still in it. A much more effective method is by sulphur dioxide. This agent, in small proportion, is rapidly destructive to all insect life occupying bedrooms and quarters generally. It is readily prepared by burning flowers or roll sulphur in the room. One pound of sulphur to every 1,000 cubic feet of space with two hours' exposure may be considered safe. Should the house or cabin contain furnishings of value, this sulphur disinfection can be accomplished without damage to these articles, providing attention is given to the production of a dry gas. The liquid sulphur dioxide (2 pounds per 1,000 cubic feet) can be used for this purpose on a dry day without injuring fabrics of any kind. Should the air contain moisture, however, the SO_2 combines with the H_2O , forming H_2SO_4 , which is an energetic bleaching agent.

Toward the end of the epidemic in Vera Cruz Dr. del Rio provided a portable room, 8 feet long and 6 feet wide, covered with wire screen. This can be taken apart, placed in a room, the patient placed therein, and for temporary use this is a good means of limiting the infection for the time being.

It may be mentioned here that scientific experiments on either malaria or yellow fever lose considerably in value when conducted in accurately prepared quarters in cities where either of these diseases are endemic. There are so many sources of error that their elimination is to a certain extent relative. It is, however, justifiable after due precaution to do this work for positive or negative data; the gradations between the two, that so frequently appear in work of this character, should have every source of error eliminated by conducting the experiment in regions enjoying a well-established immunity to these diseases.

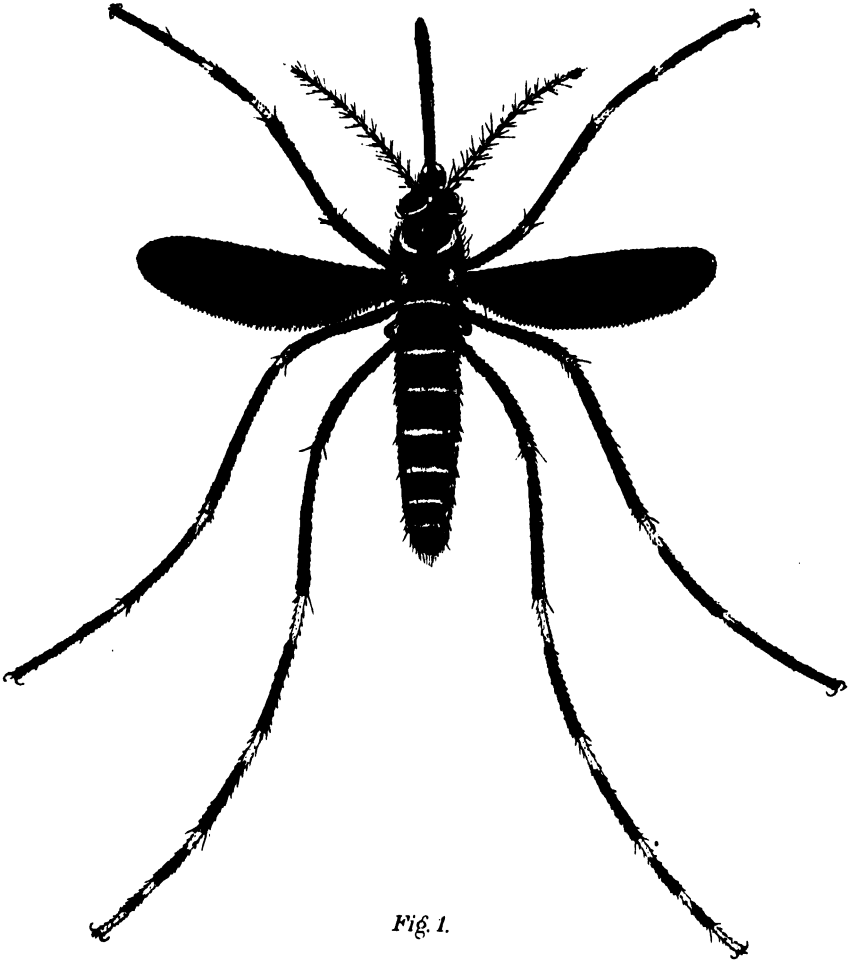


Fig. 1.

STEGOMYIA FASCIATA FABR. FEMALE.

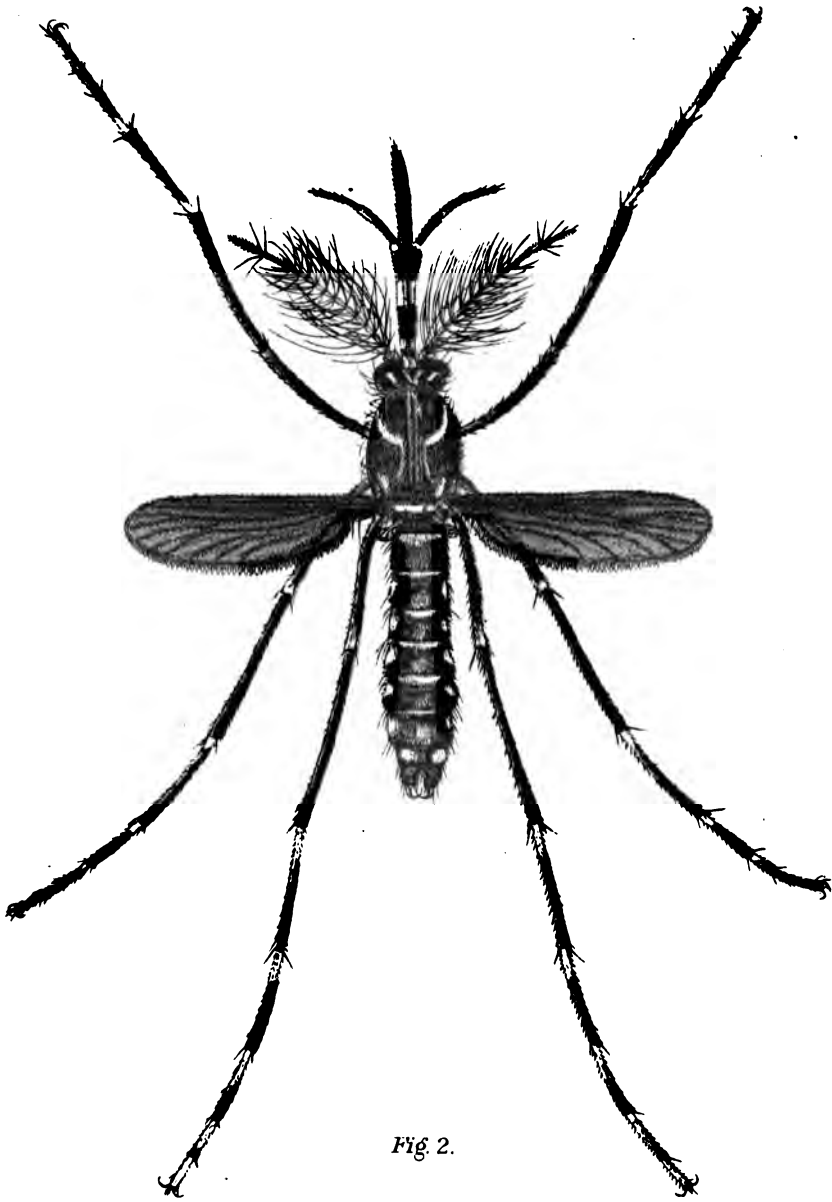


Fig 2.

STEGOMYIA FASCIATA FABR. MALE.

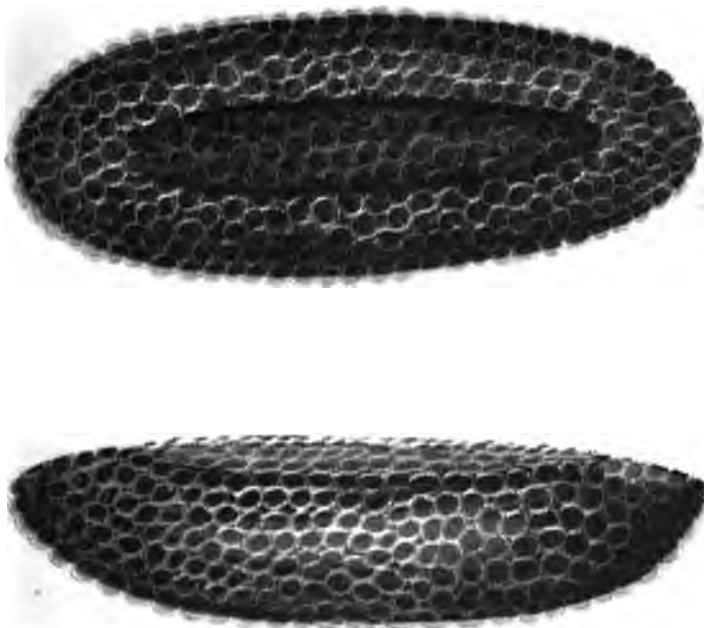


Fig.3.

EGGS OF *STEGOMYIA FASCIATA*, UPPER AND SIDE VIEW.

(AMPLIFICATION 150)

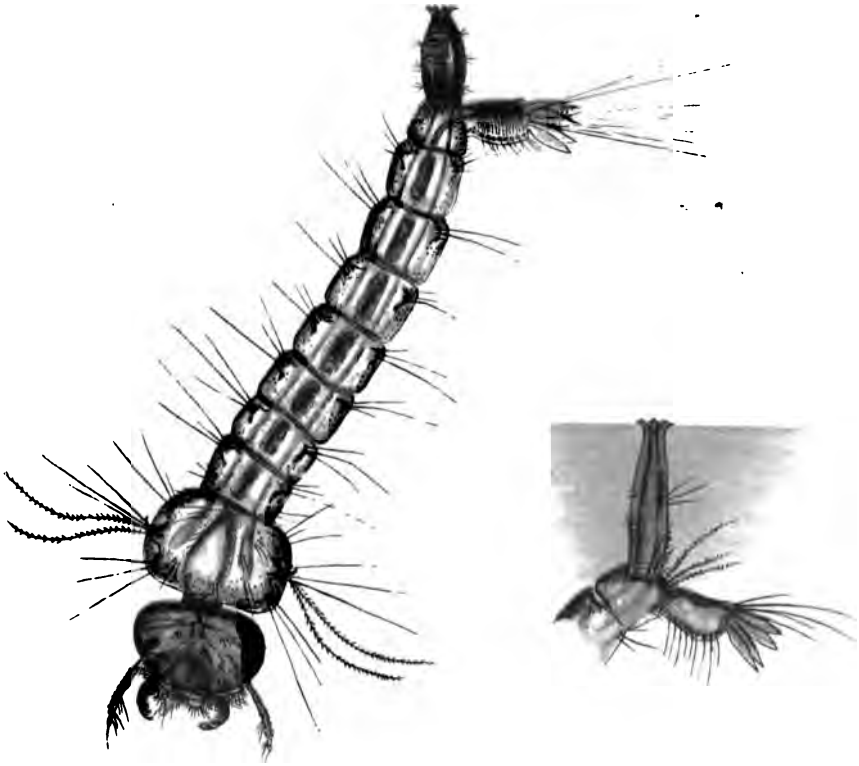


Fig. 4.

MATURE LARVA OF *STEGOMYIA FASCIATA*.
RESPIRATORY SIPHON OF *CULEX* TO THE RIGHT.



Fig. 5.

PUPA OF *STEGOMYIA FASCIATA* FABR.



FIG. 6.

SAGGITAL SECTION OF FRESH UNCONFAMINATED *STEGOMYIA FASCIATA*
SHOWING RELATION OF SALIVARY GLANDS.

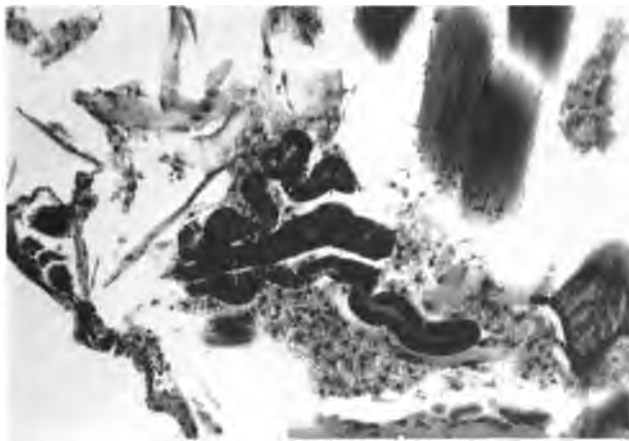


FIG. 7.

SAME AS FIG. 6, ENLARGED, SHOWING SALIVARY TUBULES IMBEDDED IN LOOSE
CONNECTIVE TISSUE; BEHIND THE TUBULES, THE PHARYNGEAL DIVERTICULUM.

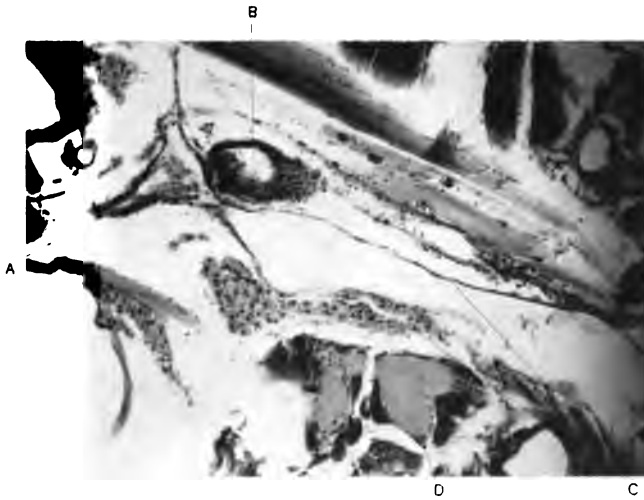


FIG. 8.

SAME MOSQUITO AS FIGS. 6, 7, SHOWING MEDIAN PLANE OF MOSQUITO,
A. ESOPHAGUS; B. HOMOLOGUE OF PROVENTRICULUS; C. UPPER
AND LOWER BORDER OF ESOPHAGEAL DIVERTICULUM;
D. THORACIC GANGLION.

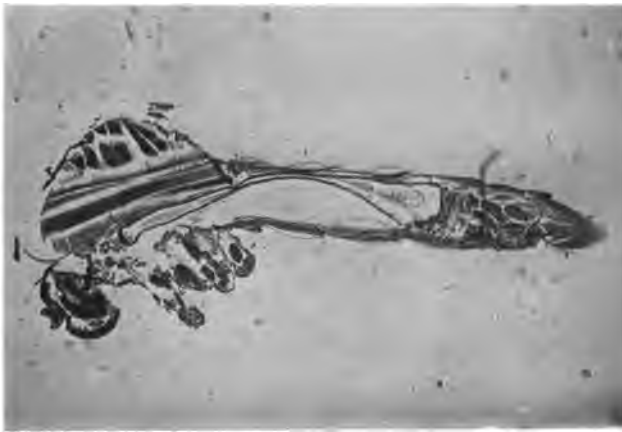


FIG. 9.

SHOWING THE WHOLE MID-GUT (THE STOMACH) THE ANTERIOR CONSTRICTED
AND POSTERIOR DILATED PORTIONS; BELOW, THE
ESOPHAGEAL DIVERTICULUM.

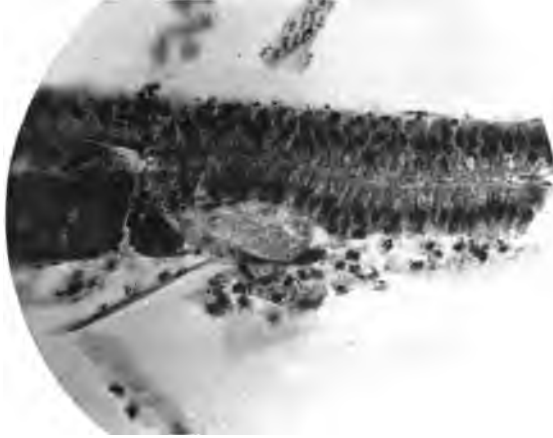


FIG. 10.

EPITHELIUM OF MID-GUT, THE TWO LAYERS IN CONTACT.



FIG. 11.

NORMAL *Stegomyia Fasciata* SHOWING ANATOMY OF HIND-GUT: A, ESOPHAGEAL DIVERTICULUM. B, MID-GUT. C, PYLORIC DILATATION. D, COLON DILATATION. E, RECTAL DILATATION AND GLANDS.



FIG. 12.

NORMAL STEGOMYIA FASCIATA SHOWING RECTUM AND RECTAL GLANDS.



FIG. 13.

MATURE OVA OF NORMAL BLOOD-FED INSECT.



FIG. 14.

NORMAL MUSCLE PLATES OF THORAX OF *Stegomyia Fasciata*.

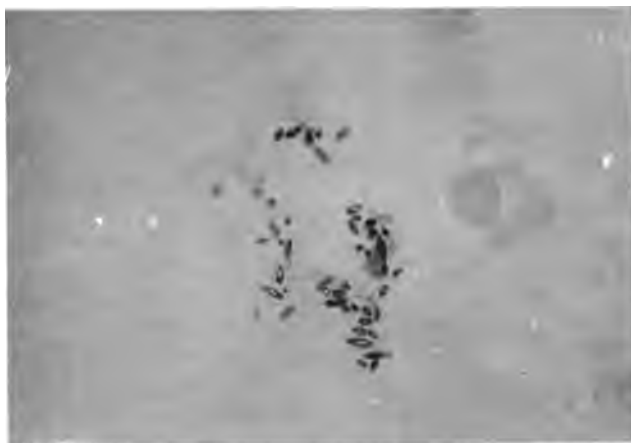


FIG. 15.

FUSIFORM SHAPE PROTOZOA, THE MYXOCOCCIDIUM STEGOMYIAE, ,
IN STOMACH AND ESOPHAGEAL DIVERTICULUM.

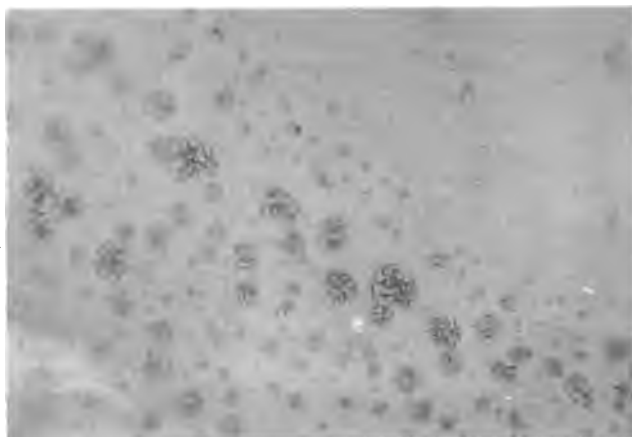


FIG. 16.

FRAGMENTATION OR MULTIPLE DIVISION OF THE (ZYGOTE?) AFTER GAINING
ENTRANCE TO THE ALBUMINOID MASS.

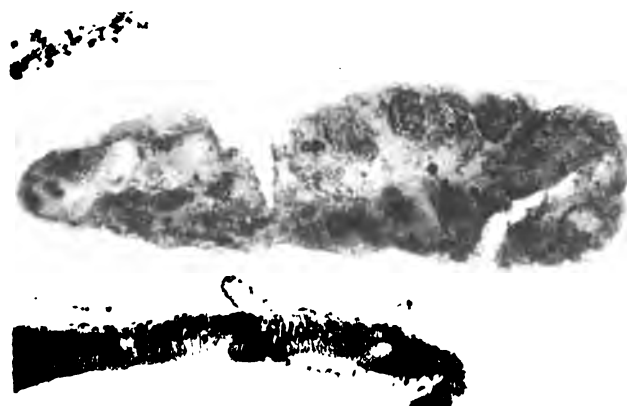


FIG. 17.

SURFACE OF ALBUMINOID MASS SHOWING MATURE AGGREGATIONS
(OOCYSTS?) OF SPOROBLASTS?



FIG. 18.

SAME MOSQUITO AS FIG. 17, SHOWING INTERIOR OF ALBUMINOID MASS.



FIG. 19.

SAME SECTION AS FIGS. 17-18 SHOWING CENTRE OF ALBUMINOID MASS.

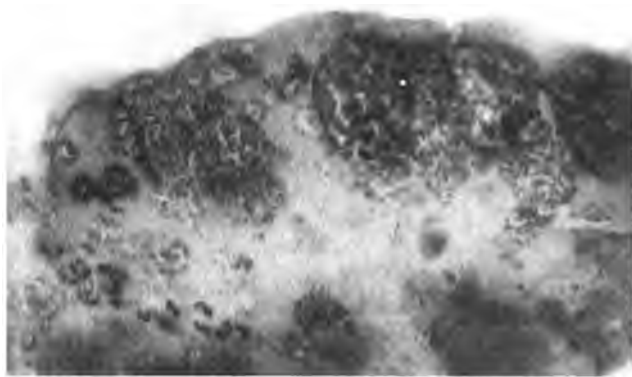


FIG. 20.



FIG. 21.

SAME AS FIG. 17, MORE HIGHLY MAGNIFIED SHOWING OOCYSTS? AND SPOROBLASTS?

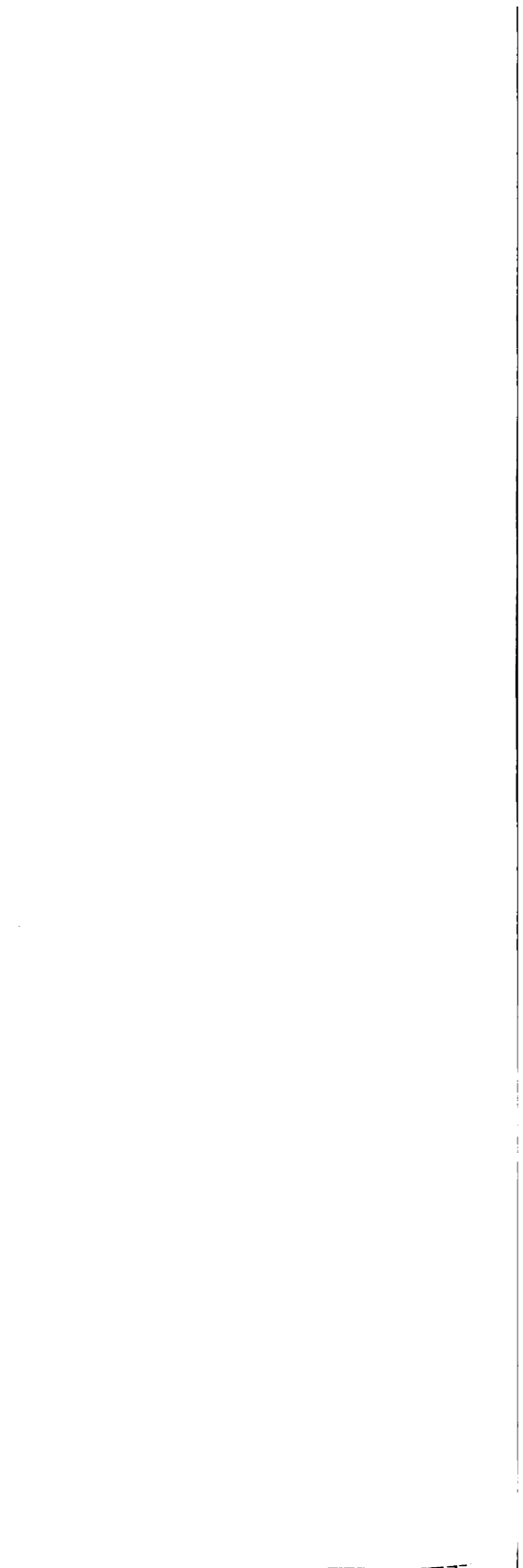




FIG. 22.



FIG. 23.



FIG. 24.

3. CYST: WITH LOW, MEDIUM AND HIGH MAGNIFICATION SHOWING
ARRANGEMENT OF SPOROBLASTS?

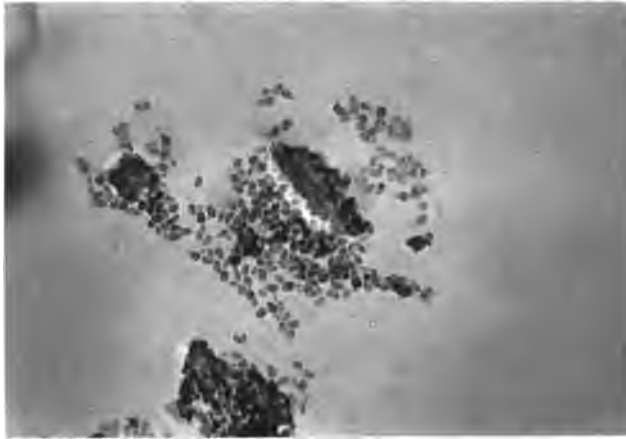


FIG. 25.

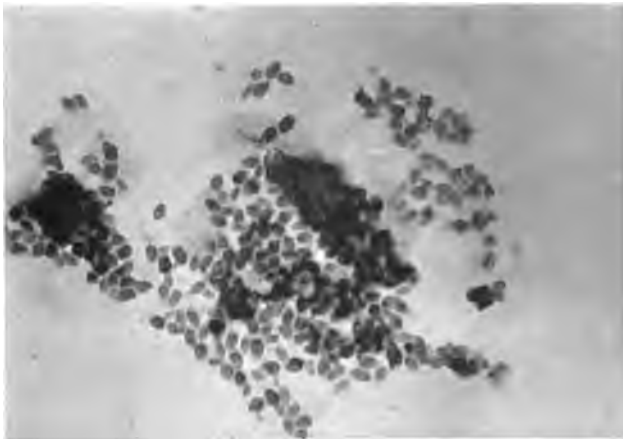


FIG. 26.

SHOWING THE DEVELOPMENT OF THE RESTING SPORE.

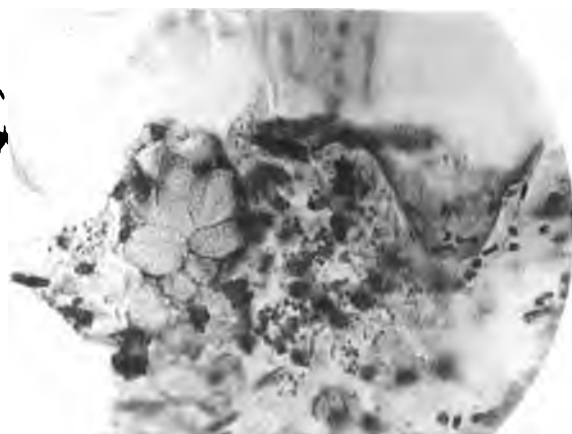


FIG. 27.

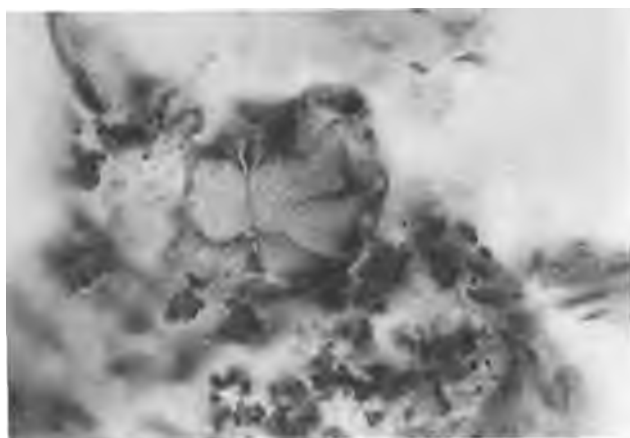


FIG. 28.

FIGURE 28. SHOWS THE "POKORNIKASIS" DISSEMINATED THROUGHOUT THE CONNECTIVE TISSUE SUPPORTING THE SALIVARY GLAND.



Fig. 29.



Fig. 30.

Fig. 29. 30. SHOWING THE "SPORE?" CONTAINING THE SPOROZOITE? IN THE SALIVARY GLAND CELLS.

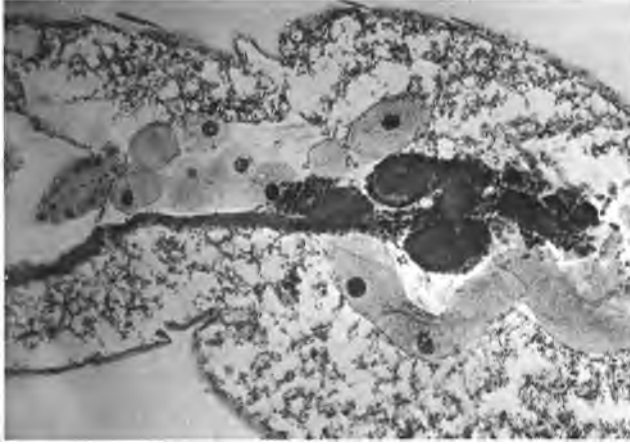


FIG. 31.

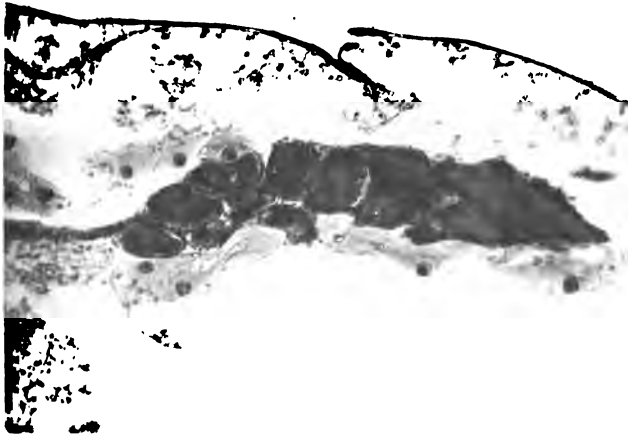
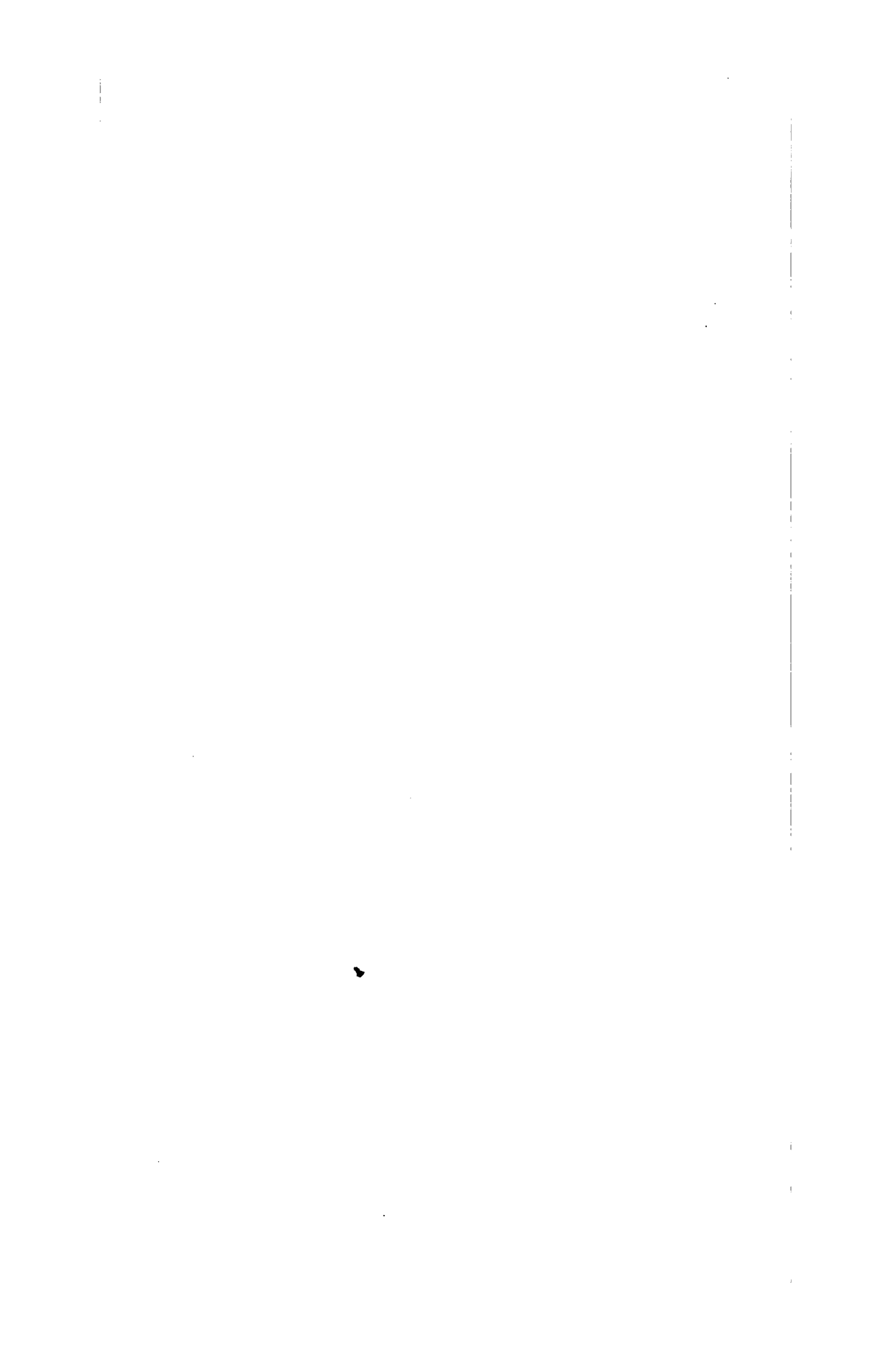


FIG. 32.

SHOW DEGENERATION OF OVA IN CONTAMINATED MOSQUITOES.



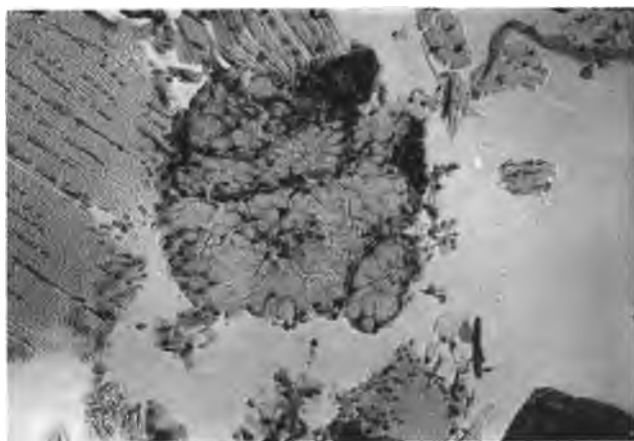


FIG. 33.

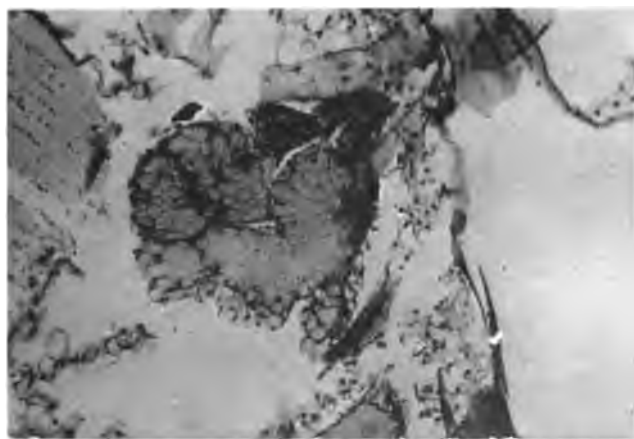


FIG. 34.

SHOWING HYPERTROPHY AND CONVOLUTIONS OF SALIVARY GLANDS
OF CONTAMINATED INSECTS.

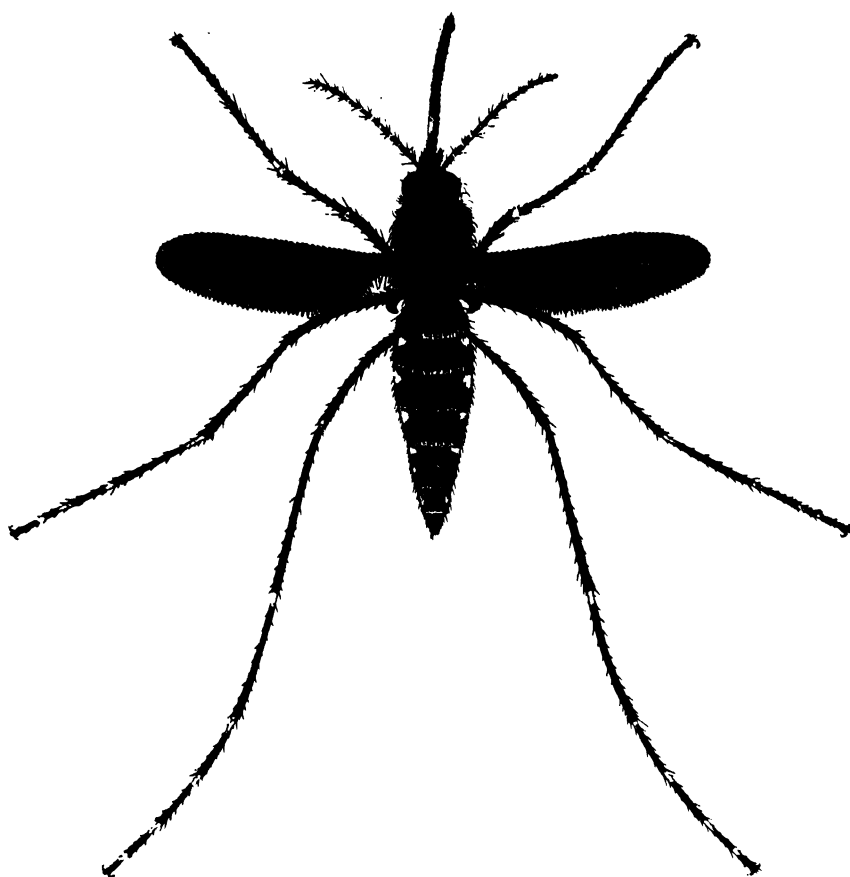


Fig. 35.

CULEX TAENIORHYNCHUS WIEDEM-FEMALE.

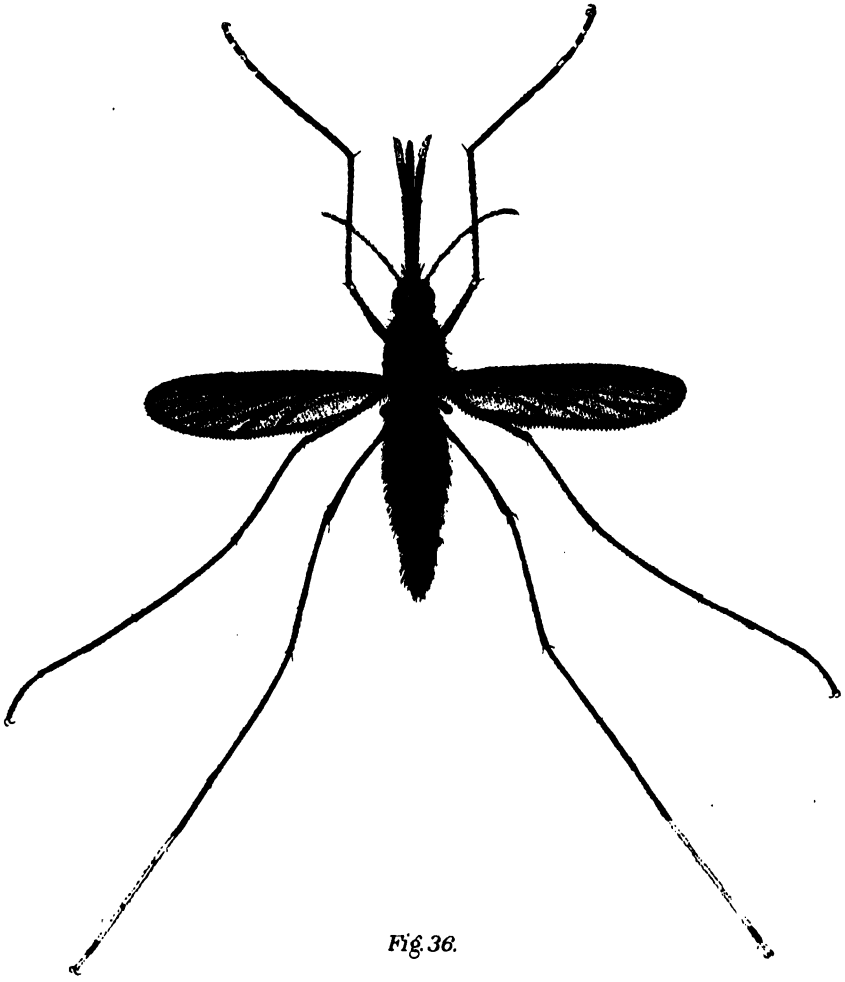


Fig. 36.

ANOPHELES ARGYROTARSIS DESV.
SUBSPECIES: ALBIPES THEO.

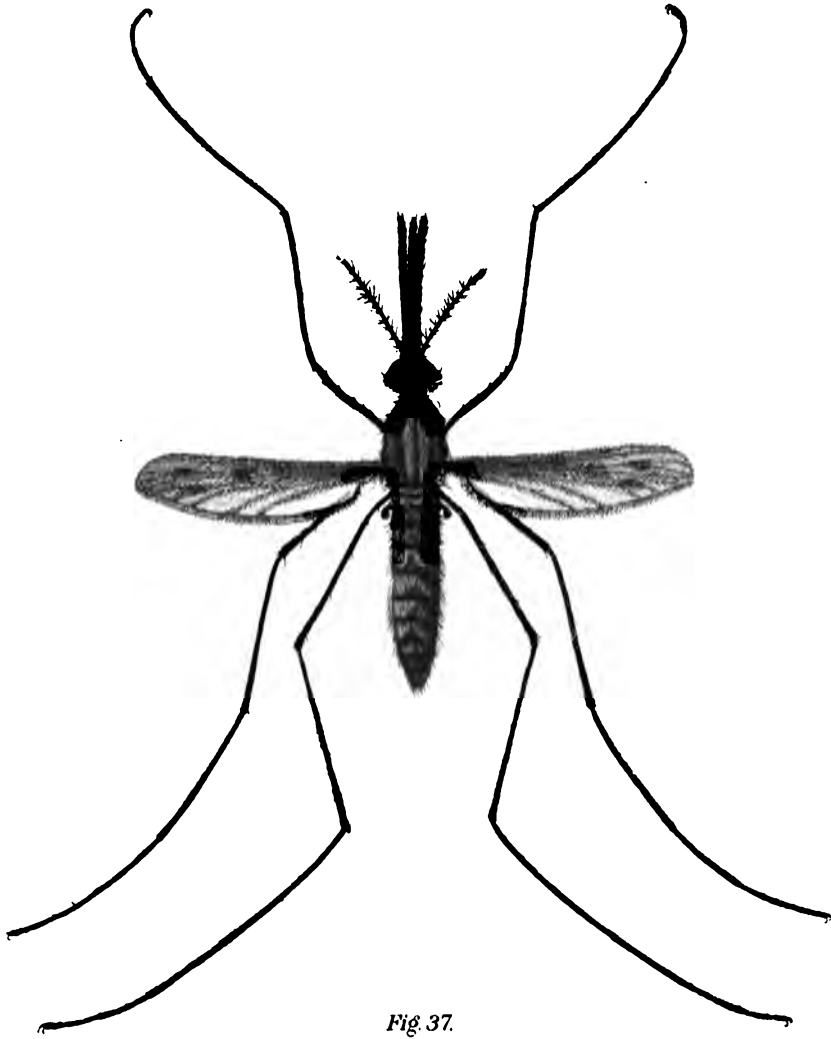


Fig 37.

ANOPHELES MACULIPENNIS MEIGEN.

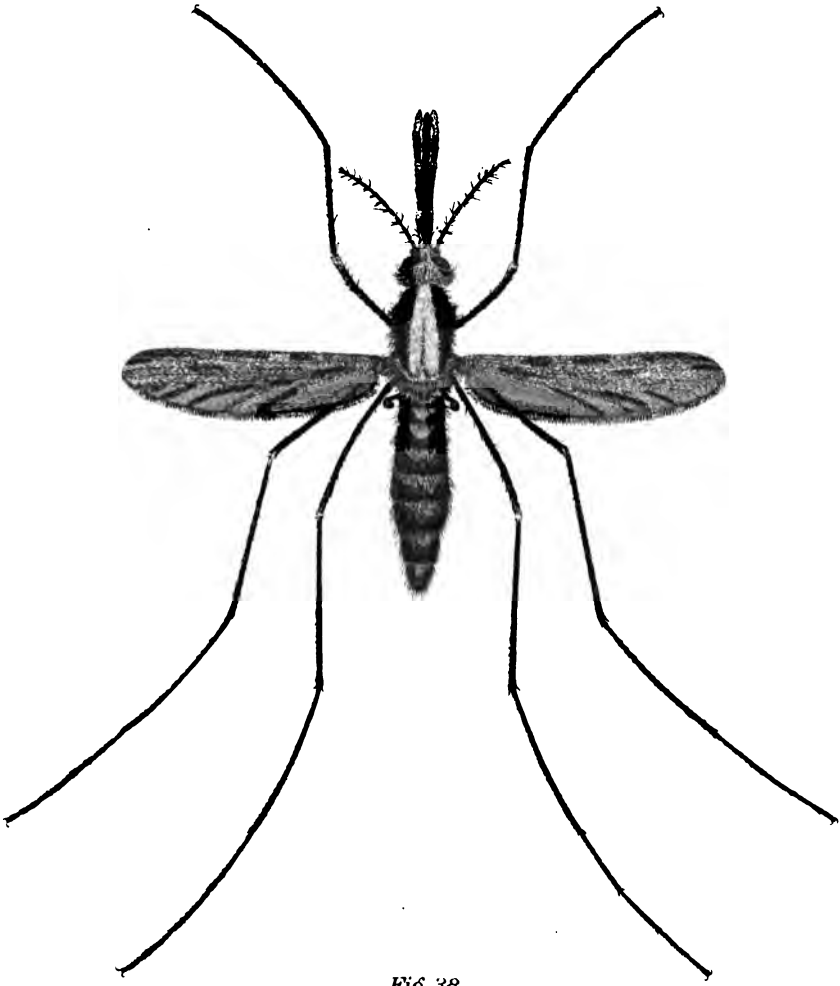


Fig. 38.

ANOPHELES PSEUDOPUNCTIPENNIS THEOBALD.

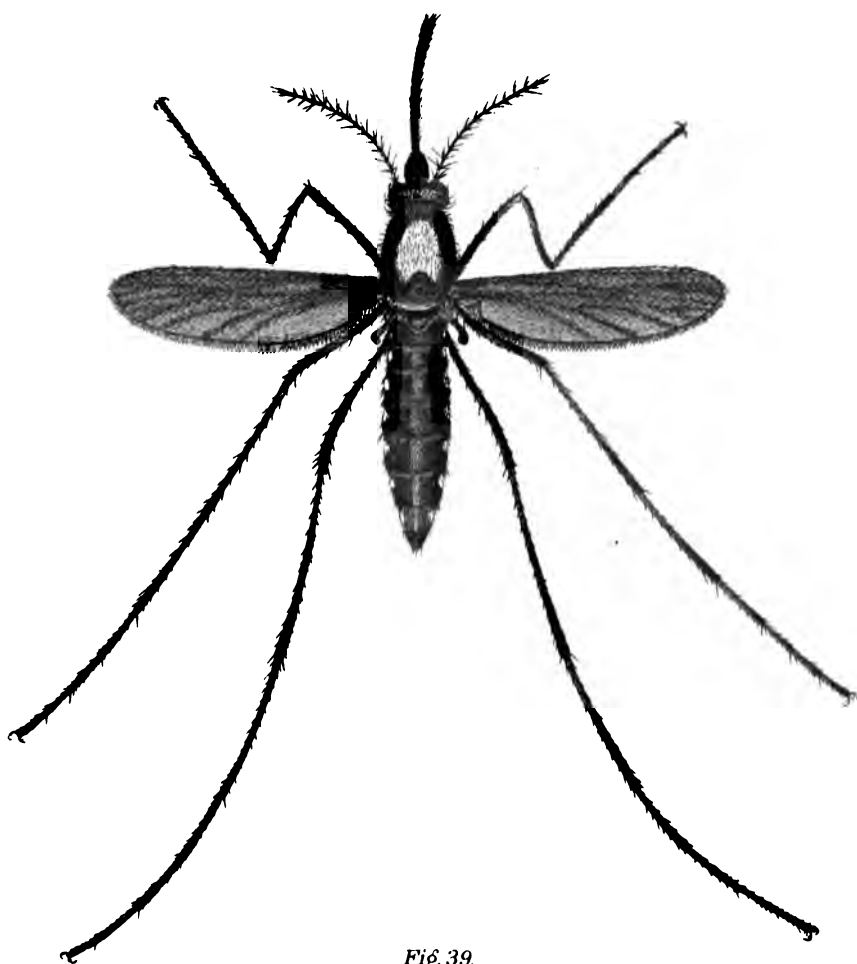


Fig. 39.

CULEX CONFIRMATUS.
(ARRIBALZAGA)

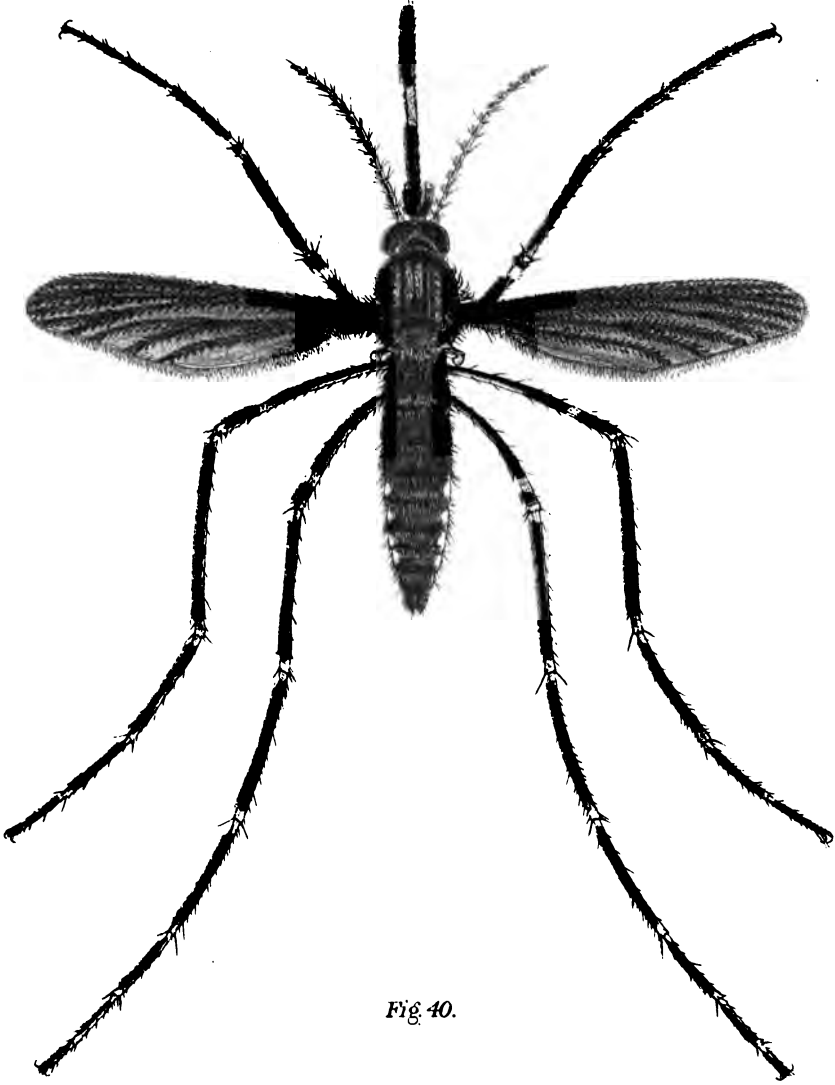


Fig 40.

TAENIORHYNCHUS FASCIOLATUS (ARRIBALZAGA).

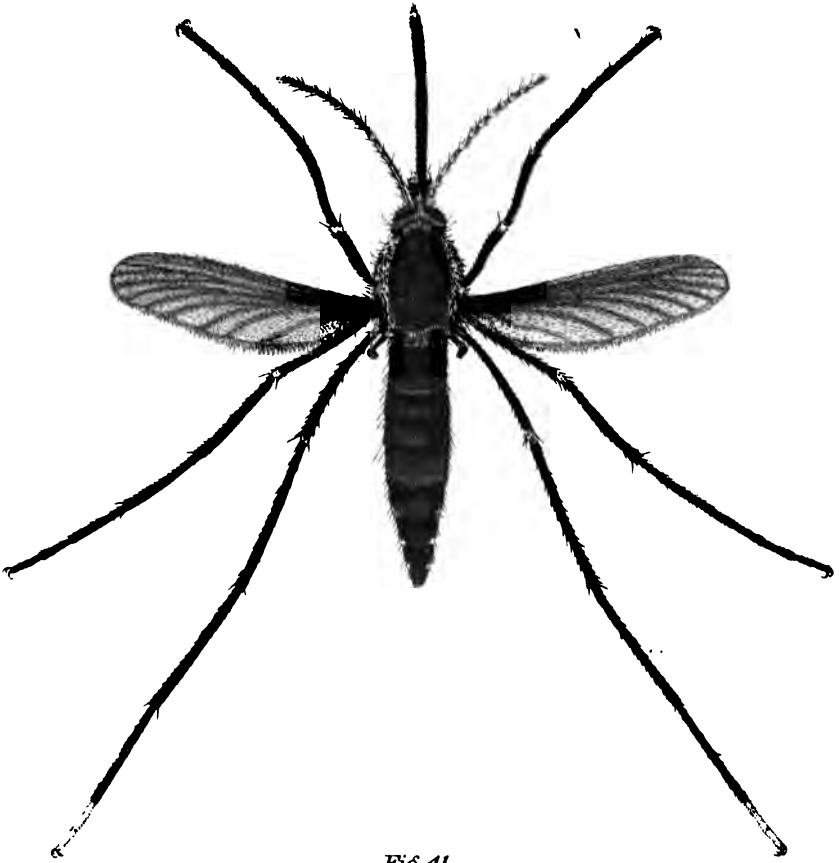


Fig. 41.

JANTHINOSOMA LUTZII ARRIBAL.

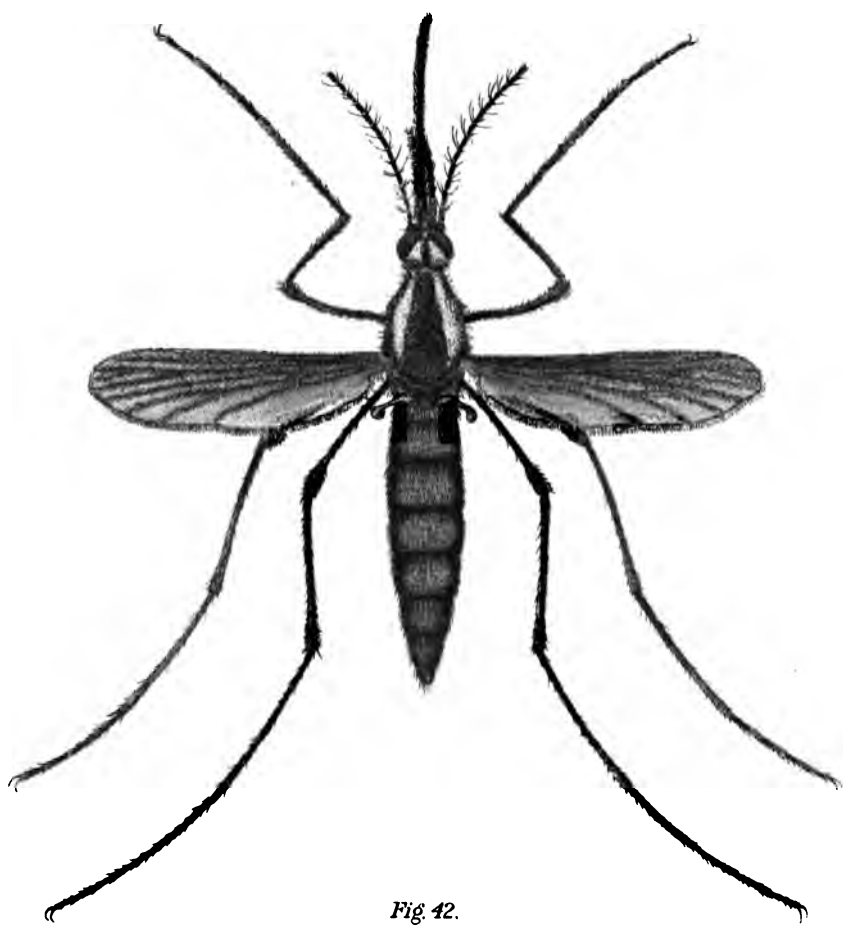


Fig 42.

PSOROPHORA SCINTILLANS ARRIBALZAGA.

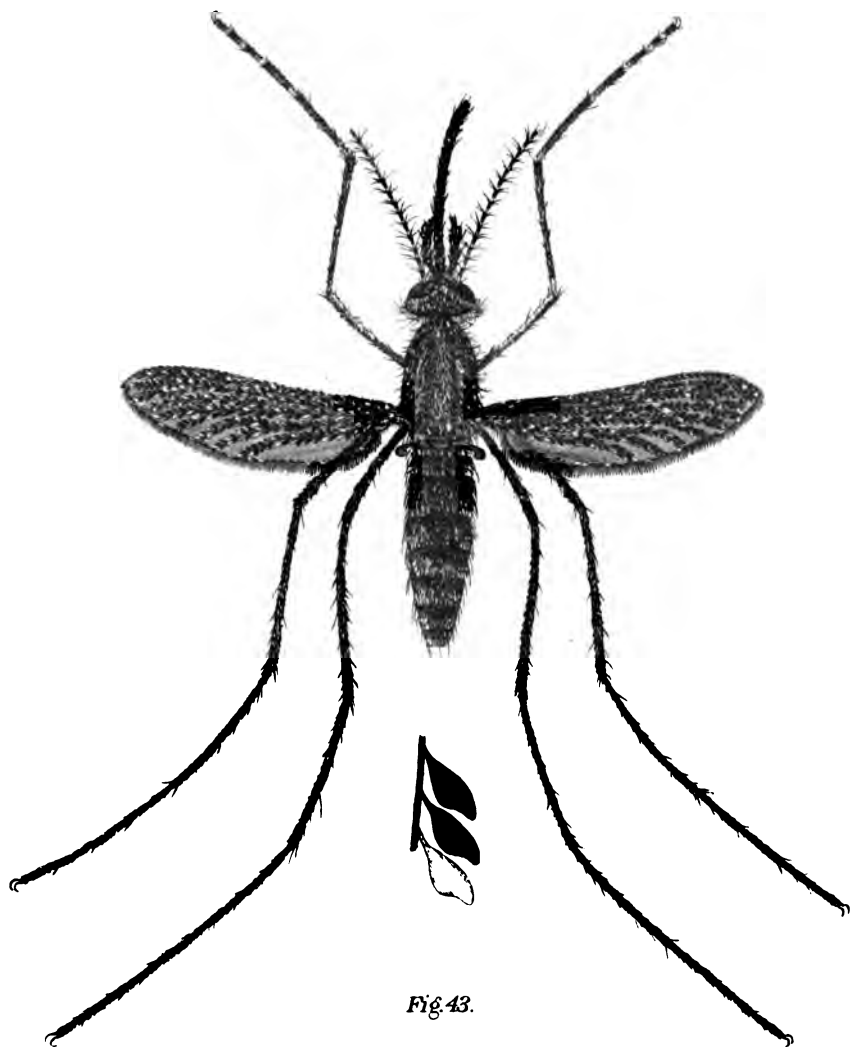


Fig. 43.

PANOPLITES PSEUDOTITILLANS THEOBALD.
WINGS CALES BELOW.

YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 14.

Section B.—ETIOLOGY.

P. A. Surg. M. J. ROSENAU, Chairman of Section.

EXPERIMENTAL STUDIES IN YELLOW FEVER AND MALARIA:

By M. J. ROSENAU, *Passed Assistant Surgeon*,
HERMAN B. PARKER, *Passed Assistant Surgeon*,
EDWARD FRANCIS, *Assistant Surgeon*,
GEORGE E. BEYER, *Acting Assistant Surgeon*.

THE CAUSE OF YELLOW FEVER.

The cause of yellow fever is not known, but we have to consider the *Myxococcidium stegomyia* of Parker, Beyer, and Pothier. These authors described in some detail the life cycle of a supposed animal parasite in infected mosquitoes closely resembling coccidia.

It was our first duty to investigate the merits of this announcement.

We therefore first sectioned about one hundred normal mosquitoes, *Stegomyia* and *Culex*, both male and female. A study of these slides soon convinced us that bodies resembling *Myxococcidium stegomyiae* may be found in normal mosquitoes and that for the most part these bodies were yeast cells in various stages of reproduction. Carroll had called our attention to this in a conversation and subsequently discussed it in an article published in the Journal of the American Medical Association for November 28, 1903.

Since then the French commission, working at Rio de Janeiro,^a has come to the same conclusion.

^a Marchoux, Salimbeni, and Simond: La fièvre jaune; rapport de la mission française. Ann. de Inst. Pasteur, tome XVII, November, 1903.

EXPLANATION OF PLATE 1.

Wild yeasts in pure culture isolated from banana at Vera Cruz, Mexico, in the summer of 1903. Stained with hematoxylin and eosin.

All the specimens show deeply stained granules.

1. Shows the lemon-shaped budding forms of *Saccharomyces apiculatus*.
- 2 and 4. Other budding forms.
3. Well marked granules.
5. Ovoid forms with granules.
6. Filamentous yeast.

Schaudinn^a considers yeasts as normal commensals of all mosquitoes and believes they play an important part in the physiology of the insect, generating the gas that is almost always found in the esophageal diverticulum and also producing an enzyme or other irritating substance which, when injected under the skin of man, causes the inflammation resulting from mosquito bites. Schaudinn considers these yeast cells to play a very important part in the economy of the insect and believes them to be hereditarily passed from the adult through the egg to the larvæ and pupæ.

Mosquitoes fed upon fruits have many more yeast cells in their bodies than those fed upon blood or other material. This we were able to confirm. We also fed mosquitoes upon pure cultures of wild yeasts growing upon banana, and found that the insects fed on such a fermenting diet would soon be so swelled up with gas that their bodies looked like transparent air bubbles. Insects so fed do very badly and it is difficult to keep them alive over a week in tropical temperatures.

Some of these wild yeasts are very interesting; one in particular—the *Saccharomyces apiculatus*, which is found widely spread throughout nature especially on fruit. This particular yeast assumes at times characteristic spindle or lemon shapes, with a bud at the pointed end, somewhat resembling one of the conjugating forms of protozoan organisms with which it has been confused.

We were enabled to isolate this yeast in pure culture from the bananas at Vera Cruz only after some difficulty. The ordinary plate methods failed because the other *saccharomyces* overgrew the small colonies of *S. apiculatus*. The following expedient finally succeeded: The overripe and fermenting piece of banana containing the morphologic forms desired is planted into orange juice. This culture medium was made by simply squeezing the oranges, taking care not to get any of the oil of the peel, then filtering until clear, and sterilizing by heat in test tubes. As the *Saccharomyces apiculatus* is a bottom yeast, the growth which appears at the bottom of the test tube in twelve to eighteen hours is examined under the microscope and, if the proper forms are found, transferred to another tube containing orange juice. This is repeated until a number of subcultures are made, and as the *Saccharomyces apiculatus* grows better in the orange juice than the other yeasts, the latter are quickly left behind until a pure culture is obtained.

We have noted in stained preparations of these wild yeasts that they sometimes show red chromatin (?) granules in a blue protoplasm

^a Schaudinn, Fritz 1904, Generations- und Wirtswechsel bei *Trypanosoma* und *Spirochaete* (vorläufige Mitteilung.). Arb. a. d. k. Gesundheitsamte, Berl., 4°.

when stained with polychrome methylene blue, such as Goldhorn's. We call attention to this, for isolated yeast bodies of this character stained thus might lead to errors of interpretation.

THE BLOOD IN YELLOW FEVER.

We are fully justified in concluding that in the blood of yellow-fever cases there is a living entity floating free in the plasma and capable of reproducing the disease. The positive results obtained in the filtration and inoculation experiments done by Reed and Carroll, corroborated by the French commission and ourselves, is sufficient proof of that statement.

We carefully examined many blood smears stained with polychrome methylene blue of Wright and Goldhorn, and failed to see the presence of any body which could be considered to stand in any causal relation to the disease.

The smears were taken from 17 cases at periods of five hours to six days after the onset of the disease. In every case blood was taken within the first three days of sickness. In several cases the blood was taken daily or on alternate days. The corpuscles and plasma were carefully searched. The red cells often showed minute blue bodies, usually round and sometimes slightly irregular, which resemble those ascribed to cell degeneration or nuclear rests in anemia.

The mononuclear leucocytes and polymorphonuclear neutrophils often showed in their protoplasm small, round, clear spaces having a punched-out appearance. These spaces could not be made to take up any one of several stains employed. They were also found in malarial and normal blood.

In making our blood preparations we used a method devised by one of us (Rosenau) about four years ago, which has been in constant use in the Hygienic Laboratory since, and as it has proven so satisfactory in our hands we will describe it. The technique was suggested by the glass slides commonly used for this purpose. The instrument consists of a little glass apparatus we call the "spreader," made by simply welding two pieces of solid glass rods together, as shown in fig. 1. The short arm should be true, so as to lie flat when applied to the slide, and should be several millimeters shorter than the width of the slide. A drop of blood is taken from the ear or finger tip and placed upon one end of the slide in the usual manner. The spreader is then applied to the drop, and if the glass is clean the blood will at once be drawn by capillary attraction across its whole length; it is then spread by a gentle, even stroke, without undue pressure, along the

slide. Very beautiful preparations, with the corpuscles lying singly, are thus obtained.

This little apparatus can readily be made at the blowpipe.

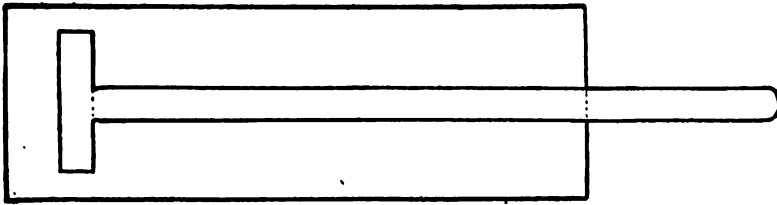
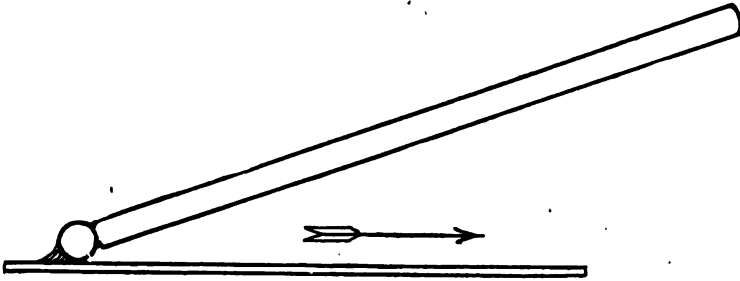


FIG. 1.—Rosenau's spreader for making blood smears.

THE PERIOD OF INCUBATION OF YELLOW FEVER.

The exact period of the incubation of yellow fever is a matter of great importance in quarantine and public-health work. For years the quarantine regulations of the Marine-Hospital Service required a detention of five days, which was considered amply safe to cover the period of incubation of the disease. The regulations of the Public Health and Marine-Hospital Service, promulgated August 10, 1903, lengthened the time of observation in special cases to six days, basing this action upon the recent experimental work which has made it possible to determine the period of incubation of yellow fever with great exactness.



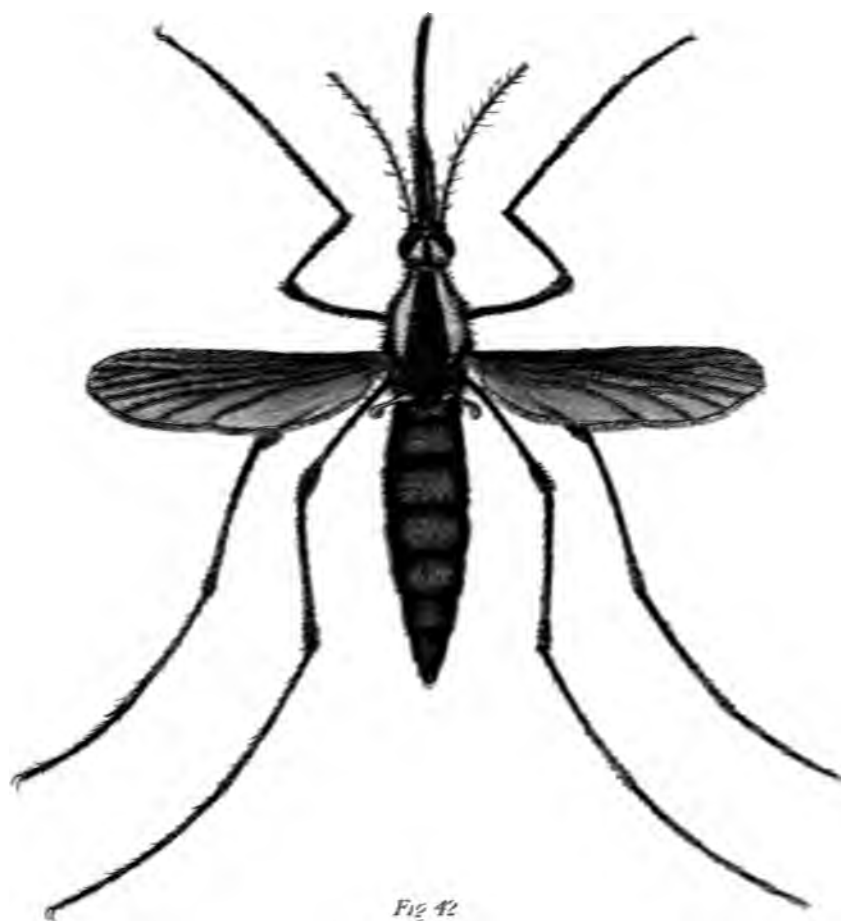


Fig 42

PSOROPHORA SCOTT LANE ADD BALZAGA

1

TABLE 1.—*Period of incubation in yellow fever, etc.—Continued.*

[Reed, Carroll, and Agramonte: "The etiology of yellow fever; an additional note," Journ. Am. Med. Assoc., Feb. 16, 1901.]

Case No.—	Bitten.	Attack.	Incubation.
15 (1).....	Dec. 5, 2 p. m.....	Dec. 8, 11.30 p. m.....	8 days 9½ hours.
16 (3).....	Dec. 8, 4 p. m.....	Dec. 14, 9 a. m.....	4 days 30 hours, took to bed; 5 days 17 hours, onset of fever.
17 (4).....	Dec. 9, 10.30 a. m.....	Dec. 12, 9.30 p. m.....	3 days 11 hours (about).
18 (5).....	Dec. 11, 4.30 p. m.....	Dec. 15, noon.....	3 days 19½ hours (bed).
19 (7).....	Bitten several times—Dec. 21, noon, and Dec. 22, 4.30 p. m.	Dec. 25, noon.....	2 days 19½ hours since shortest, and 4 days since longest exposure.
20 (6).....	Dec. 30, 11 a. m.....	Jan. 8, 10.30 a. m.....	8 days 22½ hours.

[Reed: "Experimental yellow fever," Am. Med., July 6, 1901.]

Case No.—	Bitten.	Attack.	Incubation.
21.....	Jan. 19, 3.30 p. m.....	Jan. 23, 3 p. m.....	8 days 23½ hours.
22.....	Jan. 31, 9.30 a. m.....	Feb. 3, noon.....	8 days 2½ hours.
23.....	Jan. 6, 11 a. m.....	Feb. 9, 5 p. m.....	3 days 6 hours.
24.....	Jan. 7, 2 p. m.....	Feb. 10, noon.....	2 days 22 hours.

[Reed and Carroll: "Etiology of yellow fever; a supplemental note," Am. Med., Feb. 22, 1902.]

Case No.—	Bitten.	Attack.	Incubation.
25 (1).....	Sept. 16, 4 p. m.....	Sept. 19, 4.30 p. m.....	8 days ½ hour.
26 (2).....	Oct. 9, 4 p. m.....	Oct. 13, midnight.....	3 days 8 hours (about).

[Guit  ras: Revista de Med. Trop., vol. 2, No. 10, 1900-1901.]

Case No.—	Bitten.	Attack.	Incubation.
27 (2).....	Feb. 23, 2.45 p. m.....	Feb. 26, (?) p. m.....	8 days 10 hours (about).
28 (30).....	Aug. 8, 8.30 p. m.....	Aug. 12, (?) p. m.....	4 days 5 hours.
29 (31).....	Aug. 8, 9.30 p. m.....	Aug. 11, (?) p. m.....	3 days 3 hours.
30 (33).....	Aug. 9, 9 a. m.....	Aug. 14, (?) p. m.....	5 days 8 hours.
31 (37).....	Aug. 13, 1.45 p. m.....	Aug. 17, (?) 6.45 p. m.....	3 days 19 hours.
32 (30).....	Aug. 14, 9 a. m.....	Aug. 18, (?) 6 a. m.....	3 days 21 hours.
33 (40).....	Aug. 14, 10.15 a. m.....	Aug. 20, forenoon.....	5 days 21 hours (about).
34 (41).....	Aug. 22, 4.30 p. m.....	Aug. 25, (?) 4.30 p. m.....	3 days.

[Parker, Beyer, and Pothier: "A study of the etiology of yellow fever," Yellow Fever Institute, Bull. No. 13, March, 1903.]

Case No.—	Bitten.	Attack.	Incubation.
35.....	Sept. 4, 9.30 a. m.....	Sept. 7, (?) a. m.....	8 days 2 hours (about).

[Marchoux, Salimbeni, and Simond: "La fi  vre jaune," Rapport de la Mission Francaise, Institut Pasteur, Annales, November, 1903.]

Case No.—	Bitten.	Attack.	Incubation.
36 (2).....			8 days 18 hours.
37 (17) ^a			3 days 22 hours.
38 (20).....			5 days 22 hours.
39 (22) ^b			7 days 5 hours.

^a Before being bitten by infected mosquitoes patient had received injections of blood from yellow fever cases to induce immunity: 5 cc. blood twelve days old; followed fifteen days later by same quantity eight days old.

^b This man previously had been given 20 cc. serum taken on the eighth day and passed through a Berkefeld filter; six days later 20 cc. of same serum not filtered; subsequently bitten by infected mosquitoes. The serum injections may have induced a partial immunity, which delayed the onset and modified the disease, for he had a mild attack.

TABLE 1.—*Period of incubation in yellow fever, etc.*—Continued.

[Francis and Beyer.]

Case No. —	Bitten.	Attack.	Incubation.
40.	Sept. 11, 9 a. m., and Sept. 12, 2.30 p. m.	Sept. 14, 3.30 p. m.	8 days 7 hours, or 2 days 1 hour.

A study of the 40 cases in this table discloses the fact that yellow fever usually begins about three days after the mosquito bites.

The period of incubation resulting from this natural method of conveying the disease is rarely under three days. We have but one such authentic instance, namely, two days twenty-four hours (case No. 24).

The longest period observed was seven days five hours, but it must be noted that the man who had this unusually long period of incubation had previously been treated with injections of immunizing sera, which may have delayed the onset and modified the disease, for he had a mild attack.

Leaving this case (No. 39) out of consideration, the longest period of incubation resulting from the bites of mosquitoes is the case (No. 14) of Reed, Carroll, Argamonte, and Lazear, in which an incubation period of six days two hours was observed. This corresponds strikingly to Carter's clinical observations in which he reports a case with an incubation period of five and three-fourths days. See case No. 12 in Table 1.

The French commission, working in Rio de Janeiro, came to the conclusion that the period of incubation of the disease may be much longer than this; but we find on analyzing their work that they drew their inferences largely from the disease produced by such artificial means as the inoculation of modified blood serum.

One of the conclusions of this commission was that yellow fever may not infrequently incubate for twelve days before symptoms declare themselves.

They state that "this incubation of twelve days is not absolutely rare. We have had occasion to see that the natural infection may also present an incubation equally long."

With this statement we must take issue, for the long experience of the Public Health and Marine-Hospital Service in the many wars it has waged against yellow fever has amply demonstrated that for practical purposes five days is sufficient to cover the period of incubation of the great majority of cases. An analysis of all the cases reported in Table 1 supports this view.

The French Commission reports several cases in support of their contention. One, a young man 18 years old, who took yellow fever ten days after having arrived in Petropolis from Rio de Janeiro. Petropolis is a village free from yellow fever. Another instance

was a girl 12 years old, who was taken with yellow fever ten days after returning from Rio, her father having sent her to Petropolis because his wife and three other children had the fever.

We do not doubt that Petropolis is "indemne," free of *Stegomyia fasciata*, and that the disease has never been known to spread there; but the communication with Rio is close, and if yellow fever cases are brought to Petropolis it is conceivable that infected mosquitoes may also be carried. There are many other "loopholes" which weaken observations of this kind, and we have therefore refrained from placing them in our table.

The last case cited by the French commission is as follows:

On board the vessel *Messageries*, returning to Europe, having taken passengers from Rio de Janeiro, an isolated case of yellow fever declared itself among the latter passengers between Dakar and Lisbonne; that is, nine to fourteen days.

It was our experience that some cases of yellow fever are so mild that they are detected with difficulty, especially under such unfavorable conditions as on board ship. "The isolated case" on board the *Messageries* may have been the second case, especially as the fourteen days is sufficient to cover the "extrinsic incubation" of the disease. The literature has several instances of such cases. They should be carefully considered before drawing definite conclusions.

It is interesting to compare the period of incubation resulting from exposure to infection in the "natural" way with the period of incubation resulting from experimental yellow fever, produced by the inoculation of blood or blood serum. The following table shows 17 such cases:

TABLE 2.—*Period of incubation in yellow fever, resulting from the injection of blood.*

[Reed, Carroll, and Agramonte: "Experimental yellow fever," Am. Med., July 6, 1901.]

Case No.—	Inoculated.	Attack.	Incubation.
1.....	Jan. 4, 11 a. m.....	Jan. 8, 9 a. m.....	3 days 22 hours.
2.....	Jan. 8, 9 a. m.....	Jan. 11, 9 a. m.....	2 days 12 hours.
3.....	Jan. 22, 1 p. m.....	Jan. 24, 9 a. m.....	1 day 19 hours.
4.....	Jan. 25, 12.45 p. m.....	Jan. 28, 1.15 p. m.....	3 days 1 hour.

No. 1 received subcutaneously 2 cc. blood taken on second day.

No. 2 received subcutaneously 1.5 cc. blood taken 12 hours after beginning of attack.

No. 3 received subcutaneously 0.5 cc. blood taken on second day.

No. 4 received subcutaneously 1 cc. blood taken 27½ hours after commencement of disease.

[Reed and Carroll: "The etiology of yellow fever; a supplemental note," Am. Med., Feb. 22, 1902.]

Case No.—	Inoculated.	Attack.	Incubation.
5 (3).....	Oct. 15, 4 p. m.....	Oct. 20, 6 p. m.....	5 days 2 hours.

Case 5 received subcutaneously 0.75 cc. partially defibrinated blood 15½ hours old.

TABLE 2.—*Period of incubation in yellow fever, etc.*—Continued.[Reed and Carroll: "The etiology of yellow fever; a supplemental note," *Am. Med.*, Feb. 22, 1902.]

Case No.—	Inoculated.	Attack.	Incubation.
6 (7)	Oct. 15, 11 a. m.	Oct. 19, 3 p. m.	4 days 4 hours.
7 (8)	Oct. 15, 11.05 a. m.	Oct. 19, noon.	4 days 1 hour.

Cases 6 and 7 were inoculated subcutaneously with 3 cc. of an equal volume of water and serum filtered through a Berkefeld filter.

[Marchoux, Salimbeni, and Simond: "La fièvre jaune," *Rapport de la mission française, Institut Pasteur, Annales*, November, 1903.]

Case No.—		Incubation.
8 (1)	1 cc. serum	5 days 5 hours.
9 (3)	5 cc. serum heated to 55° for ten minutes; five days later, 10 cc. heated to 55° for ten minutes; seven days later, 1 cc. blood. This was a "remarkably benign case," and as the man had been injected previously with heated yellow fever serum, the immunity produced probably explains the long period of incubation as well as the mildness of the attack.	12 days 12 hours.
10 (4)	5 cc. serum heated to 55° for twenty minutes; seven days later, 10 cc. serum heated to 55° for ten minutes; eight days later, 1 cc. serum heated to 55° for five minutes. Then 1 cc. serum. The same explanation for this unusually long period of incubation as above, especially as a parallel case similarly treated showed an immunity.	8 days 5 hours.
11 (7)	1 cc. serum filtered through a Chamberland F filter	5 days 18 hours.
12 (8)	do.	12 days 18 hours.
13 (13)	0.1 cc. (1 drop) of serum	4 days 18 hours.
14 (15)	5 cc. blood, 5 days old	2 days 21 hours.

[Francis and Beyer.]

Case No.—	Inoculated.	Attack.	Incubation.
15 (2) ^a	Sept. 15, 4 p. m.	Sept. 17, (?) a. m.	1 day, 15 hours (about).
16 (3) ^b	do.	do.	Do.
17 (4) ^c	do.	Sept. 17, 9 a. m.	1 day, 17 hours.

^a Intravenous injection of 1.75 cc. serum diluted with an equal volume of salt solution and filtered through a Chamberland B filter.

^b Intravenous injection of 2.5 cc. serum diluted with an equal volume of salt solution and filtered through a Chamberland B filter.

^c Intravenous injection of 2.5 cc. serum diluted with an equal volume of salt solution and filtered through a Chamberland B filter.

It will be noted from these 17 cases that the period of incubation of yellow fever produced by the inoculation of blood or blood serum is not so constant a factor as in Table 1, in which the disease was induced by the bites of mosquitoes.

The shortest time in this table is one day fifteen hours, and the longest twelve days eighteen hours.

Surg. H. R. Carter, Public Health and Marine-Hospital Service, has given special attention to this phase of the subject, and we are indebted to him for valuable suggestions.

THE FILTRATION OF YELLOW-FEVER BLOOD.

Reed and Carroll (*Am. Med.*, Feb. 22, 1902) were the first to filter yellow-fever blood and prove the infectiousness of the filtrate. They passed it through a Berkefeld filter, which on testing held back the *Staphylococcus pyogenes aureus*.

The filtrate showed no growth in bouillon, and yet when injected into nonimmunes produced yellow fever. The blood from the latter was also shown to be capable of producing yellow fever when injected into a third subject.

That the men inoculated with the filtrate suffered from yellow fever induced by a morphologic entity which passed the filter, and not from a toxemia, was shown not only by their rather long periods of incubation, but was conclusively shown by carrying their experiment to the third degree.

The following experiments were planned in order to determine among other things whether the organism of yellow fever, as it exists in the blood serum, is capable of passing the pores of the Pasteur-Chamberland B filter:

An investigation of the literature of the other filterable viruses shows that the South African horse sickness is the only one which has yet been reported as having passed the Chamberland B filter.

In the filters of the Pasteur-Chamberland system those marked "B" are finer, more compact, with thicker walls, and consequently less porous than those marked F. We have been informed by Assistant Surgeon-General H. D. Geddings, who has recently inquired about this in Paris, that only two grades—B and F—are now being made.

The subjects used for our experimentation were all volunteers, non-immunes, and carefully selected from among the native Mexicans at Jalapa and the adjacent mountainous country, taken by train to Vera Cruz, and immediately placed within the screened wards of our hospital. All cases recovered.

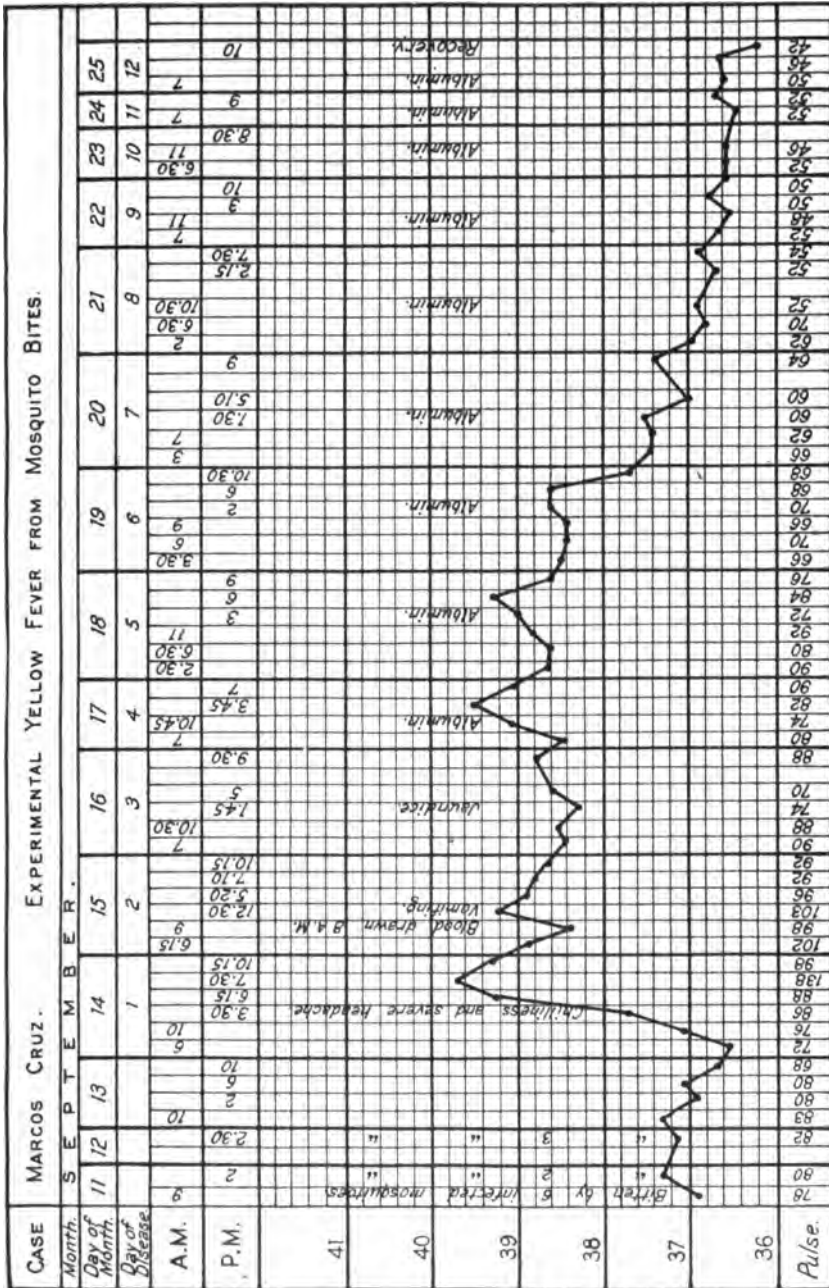
Jalapa is a town having an elevation of about 4,000 feet, where yellow fever has never been known to spread and has not existed, except for the cases occasionally imported from the coast (*tierra caliente*).

In order that the case from which we drew the blood for filtration should be one in which there was the highest degree of confidence as to the diagnosis of yellow fever, we decided to produce the disease through the bites of infected mosquitoes rather than to select a case by clinical evidence alone from the yellow-fever wards.

Mosquitos which had been allowed to feed upon typical cases of yellow fever in San Sebastian Hospital, Vera Cruz, were applied in succession to the hands of four persons whom we had selected as being nonimmunes. The first three failed to become infected, but the fourth took sick with what proved typical yellow fever. The histories of the three negative cases are here given in brief:

G. M., age 22, Mexican.—On August 13 he was taken to Vera Cruz and placed in our screened ward. August 15, at 3.20 p. m., he was bitten by two mosquitoes which had fed twelve days previously, at 9.30 a. m., on J. R., a fatal case of yellow fever. Nothing unusual





September 14, at 4 p. m., Cruz complained of feeling chilly and had frontal headache. The chilly sensation lasted for several hours and the headache became so severe that he was given ice caps to his forehead for the relief of this symptom. The conjunctivæ became injected; the gums turgid and red.

The case continued clinically with typical symptoms of yellow fever.

On September 15, at 8 a. m., there was a slight icterus of the eyes; at 10 a. m. there was marked vomiting; at 7 p. m. the gums were very much swollen. Urine contained no albumin.

September 16: Eyes injected and yellowish, skin jaundiced; no albumin.

On September 17, the third day of the disease, albumin first appeared in the urine and was found daily until September 25, after which examination was discontinued.

On September 15, at 8 a. m., 16 hours after the onset of the disease 80 cc. of blood were drawn into a sterile flask by means of an aspirating needle from the median basilic vein of his left arm.

The flask was set aside in the lower part of the ice chest, at a temperature of from 16° to 19° C., for five hours in order to allow the blood to coagulate.

Thirty-five cubic centimeters of the clear serum were then drawn off, and to it was added an equal volume of physiological salt solution.

The mixture was transferred with all due precautions to the inside of a Pasteur-Chamberland B bougie and filtered from within outward by means of vacuum, which was applied to the outer surface of the filter in a reverse manner to that shown in fig. 2, omitting the paraffin cup.

It required one hour to obtain 13.5 cc. of filtrate, which was used for the injection of three nonimmunes, Bonifacio Orea, German Ramos, and Guadalupe Gomez.

Orea and Ramos each received 5 cc. of the filtrate, injected intravenously into one of the veins of the arm. As the same was diluted with an equal volume of salt solution, each man received 2.5 cc. of the original blood serum.

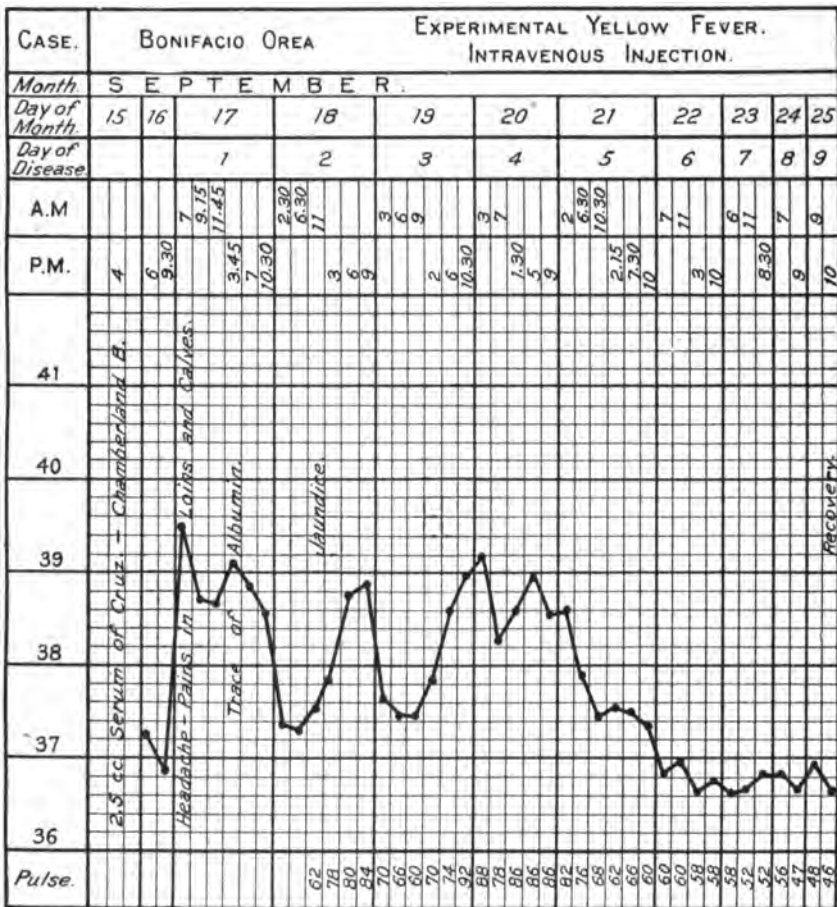
Gomez received 3.5 cc. of the mixture, representing 1.75 cc. of the original serum.

These injections were made at 4 p. m. September 15, which was just eight hours after the blood had been drawn from Cruz, the blood having kept five hours at a temperature of 16° to 19° C. and three hours at room temperature.

YELLOW FEVER PRODUCED BY THE INOCULATION OF BLOOD SERUM.

Bonifacio Orea (case LXV), aged 33, single; born in the mountains near Puebla; said that he had never been on the coast and never had any sickness of any kind. He was physically sound on examination; blood and urine negative.

He was brought to Vera Cruz August 28 and kept in a mosquito-proof room under observation for eighteen days.



Temperature chart of Bonifacio Orea.

On September 15, at 4 p. m., he was given an intravenous injection into one of his arm veins of 5 cc. of Marcos Cruz's diluted serum filtered through a Chamberland B bougie. As the serum had been diluted with an equal quantity of physiological salt solution Orea

actually received 2.5 cc. of the blood serum of Cruz. (For details of this filtration, see p. 62.)

On September 16 there were no symptoms.

September 17, at 7 a. m., he was found with a temperature of 39.5° C., with marked frontal headache, pains in the loins and calves of the legs. His gums were slightly swollen and he had injection of the ocular conjunctivæ. The patient said that at 1 o'clock in the morning he felt like stretching and had a chill. The blood showed no malarial parasites. Urine showed a trace of albumin.

September 18: Eyes and body jaundiced.

The patient made a rapid recovery after a mild but definite attack of yellow fever.

German Ramos (case L), aged 22, single; has always lived in the mountains near Puebla. He was given a careful physical examination August 26. Blood and urine negative. He was brought to Vera Cruz August 28 and immediately placed in a mosquito-proof room, where he was kept under observation eighteen days, when he was given an injection of filtered serum, as follows:

On September 15, at 4 p. m., he was given an injection into the right median basilic vein of 5 cc. of diluted serum of Marcos Cruz, filtered through a Pasteur-Chamberland filter B. This serum having been diluted with an equal volume of physiological salt solution, Ramos received 2.5 cc. of the serum of Cruz. (For details of this filtration, see the records of Marcos Cruz, page 62.)

September 16, no change.

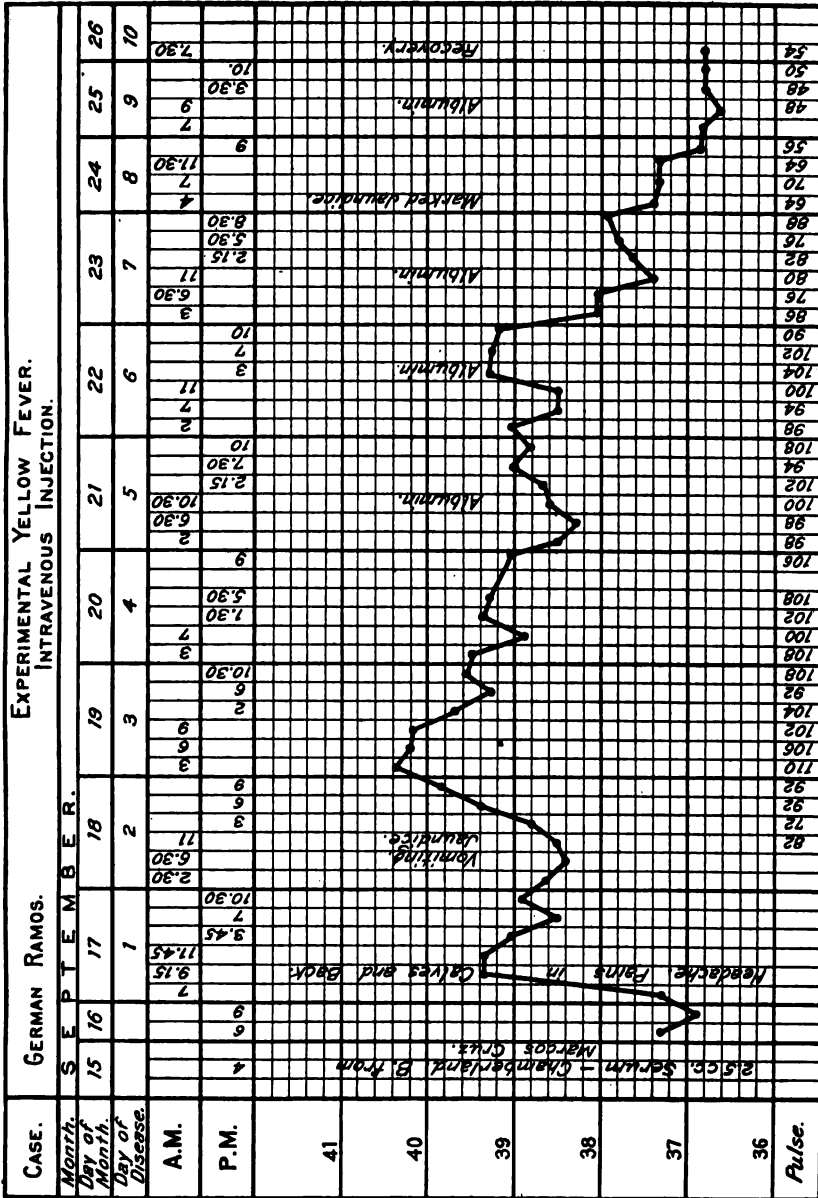
September 17, at 7 a. m., his temperature was 37.3° C., and he did not feel at all unusual; but at 9.15 a. m. his temperature was 39.4°. He had frontal headache, pains in the back and calves of the legs. The blood was negative for malaria.

September 18, the eyes were injected and the body jaundiced. Patient vomited twice. He exhibited a typical clinical picture of yellow fever.

His temperature on the third day was higher than at the onset of the disease, which is rather unusual, and in Vera Cruz is considered a grave sign. It will also be noted that his febrile period, which lasted seven days, did not show the characteristic remission. Albumin first appeared on the 21st and continued until the 25th, when examination was discontinued.

Patient recovered.

Guadalupe Gomez (case LI); born in Jalapa, aged 17, had never been on the coast, and states that he never had any kind of fever. He was physically sound when examined; blood and urine negative. He was brought to Vera Cruz August 28 and placed in a mosquito-proof room where he was kept under observation eighteen days.



REMARKS ON FILTRATION EXPERIMENTS WITH YELLOW-FEVER BLOOD.

We have been careful to give with some minuteness all the details of the manner in which the blood was filtered in these experiments. We know that the filtration of micro-organisms or other small particles through porcelain or diatomaceous earth is influenced very much by the length of time the filtration is continued, the pressure used, by the character of the fluid in which the particles are suspended, the temperature, and other factors which are perhaps less known.

Our review of the literature on the filtration of blood and body juices containing the infectious material of diseases, the causes of which are unknown and which are believed to be ultramicroscopic, disclosed reports of successful and unsuccessful filtration with such meager details that it is difficult to draw proper conclusions. Those factors which control the power of a given filter to allow an organism to pass or to hold it back also account for the different results which various experimenters have obtained in certain cases.

For instance, we succeeded in passing diluted yellow-fever serum through the closest-grained Pasteur-Chamberland B filter that we could obtain, whereas the French commission—Marchoux, Salimbeni, and Simond—working at Rio de Janeiro, failed to pass the infective agent of yellow fever through a Chamberland B filter, though they found that it did pass through the Chamberland F filter,. As the French commission used undiluted blood and we used diluted serum, the apparent discrepancy in results is accounted for; for it is a well-known fact that particles suspended in an albuminous medium filter with more difficulty than particles suspended in water, alcohol, or other limpid menstra of this character.

Nocard, Roux, and Dujardin-Beaumetz, in 1899, endeavored to repeat Löffler's experiment with apthous fever. They first failed to pass the infective agent contained in the lymph of this disease through a Berkefeld filter because they used an albuminous fluid, viz, "Martin's serum-bouillon," in order to dilute the lymph with a nutrient medium, thus hoping to obtain cultures without the danger of contamination in the filtrate. They found, however, that the albuminous matter contained in the diluting fluid clogged the pores of the filter, so that the filtrate was not virulent.

They repeated the experiment, using water to dilute the lymph in the proportion of 1 to 50, when they found the organisms causing apthous fever readily passed through a Berkefeld filter, and gave the disease by intravenous injection to young and old cattle.

It is also a well-known fact that filters which successfully hold back certain bacteria will permit them to pass if the filtration is con-

tinued long enough. In this case the organisms are believed to grow through the pores of the filter.

It is also evident that the passage of small particles through the pores of a filter depends directly upon the pressure used, and in all filtration experiments the exact pressure, whether positive or negative, should be stated.

It is further necessary to call attention to the very great discrepancy in filters. We have made a careful study of various filters found upon the market and find that there is no satisfactory method by which they can be accurately graded, although we find in certain makes an attempt to graduate the power of the filter. Filters of course should always be tested under water with air pressure for pin holes and cracks, and also with small bacteria for permeability. It is only in this way that we may determine approximately what a particular filter is capable of doing.

The Berkefeld filters, made of diatomaceous earth, are more porous and variable than the Pasteur-Chamberland bougies, made of unglazed porcelain, which have finer pores and are more constant in their ability to filter micro-organisms.

After filters have been tested they must be dried and sterilized with the greatest care in order to prevent cracking, and should always be tested for porosity with microbes after filtration in order to insure this point.

We have found in testing various filters that the weakest part is apt to be the joint, and that in any mechanical arrangement of the filter and flask there is the greatest danger of contamination and untrustworthy results if either the liquid that is being filtered or any other fluid comes in contact with a joint.

It will be noted that in the arrangement which we had for filtration by pressure (fig. 2), the fluid was simply passed into the Pasteur-Chamberland candle and withdrawn by means of a pipette in such a manner that contact between the two fluids was eliminated, and that no dependence was placed upon the security of any joints except those necessary to retain the air pressure. In the case of the small Berkefeld filter (fig. 3), in which the filtration was done by the pressure of the atmosphere produced by a vacuum, the joint between the filtering candle and the metal top was kept well out of the liquid, so that here again was avoided the possibility of error from this source.

TESTING OF FILTERS WITH OBJECTS OF "ULTRAMICROSCOPIC" SIZE.

Four filters of the Pasteur-Chamberland system, letter B, were + to determine whether they would allow particles of micro-size to pass into the filtrate.

At once we were confronted with the difficulty of finding a

substance suitable for such a purpose. The substance should be in a very fine state of division, composed of particles grading gradually in size from the ultramicroscopic to those of definite microscopic size. The substance should be insoluble in the menstrum, so that a particle recognized in the filtrate would not represent a precipitate formed after passing the filter.

We finally selected carbon on account of its insolubility, the very fine state of division into which it can be brought, and the ease with which the small particles may be recognized because of their black color and violent Brownian movement.

To 60 cc. of distilled water we added 40 drops of Higgins's American india ink, bought on the market, and this suspension was placed into each of the four Chamberland B filters and drawn through the walls from within outward by a vacuum in a reverse manner to fig. 2. The first water to come through was pale, but gradually it became slightly brown and later the surface of the filter took on a distinctly dark color. About one and a quarter hours was required for the 60 cc. to pass through each filter.

The filtrates of the four filters were examined with Zeiss microscopes, using objectives of 1.5 and 2 mm. and oculars 4 to 12, and there was not the slightest difficulty to see in the hanging drops small particles of carbon in active Brownian movement. Dried specimens of the filtrate showed small particles plainly visible.

These filters were new and were tested under pressure beneath the surface of water and found free from cracks and pin holes. Before testing with the india ink they were washed with distilled water, about 200 cc. being put through each one.

The filters first became black in disseminated points on the surface. The black areas were of irregular shape, having a diameter of one-eighth to one-fourth inch. As the filtration continued these areas became larger. At the end of the filtration the filter had a distinctly mottled appearance, showing streaks of white, small circumscribed areas of deep black, and larger areas less deeply stained. That these areas of black are carbon may be demonstrated by burning them in the flame.

This shows a lack of uniformity in the structure of each individual filter, which only confirms what may be seen after breaking a filter into pieces. At places air spaces may be seen which may extend through almost the entire thickness of the wall, thus reducing the real thickness of the filter to a mere shell.

Two new Berkefeld filters, $2\frac{1}{4}$ by $\frac{5}{8}$ inches, were tested with the dilute ink solution. Neither pressure nor vacuum was used. The filtrate came in drops in rapid succession and was as black as the test fluid and showed the particles of carbon under the microscope.

These same filters were tested with a bouillon culture of *Staphylococcus pyogenes aureus* in a reverse manner to fig. 2. From three to four hours were taken in passing 150 cc. of the bouillon culture through each filter. The filtrates remained sterile after twelve days in the incubator.

The Berkefeld filters were rigged with the glass cylinders which come with them and a vacuum was used. About four hours were required to run 150 cc. of the bouillon culture through each filter.

THE FILTRATION OF CERTAIN VIRUSES.

Peripneumonia of cattle, rinderpest, foot-and-mouth disease, South African horse sickness, exudative typhus of chickens, mosaic disease of the tobacco leaf, yellow fever, epithelioma contagiosum of fowls, hydrophobia, clavelle, and hog cholera have each been shown to be due to a virus which passes the pores of certain porcelain and diatomaceous filters which hold back the ordinary bacteria.

With the exception of peripneumonia we know nothing of the character of the infective agent in these filtrates, which by direct microscopic examination and by cultural methods have yielded no morphological entity.

The outlook for finding in the body fluids, the specific cause of any one of these diseases, by the microscopes in present use is encouraging as long as we can say that we have a filter which will not allow the virus of the disease to pass, but which does allow the particles of some test substance to be plainly seen in the filtrate.

It is far more important to know what particular filter a certain virus can *not* pass through than it is to know what brands of filter it does pass through. Given a filter that will not permit the virus of a disease to pass through its pores, and if on testing that filter we find that we can put through it visible particles of some test substance, there is plenty of hope that the infective agent of that virus may be visible with our present oil-immersion systems.

On the other hand, if we can find a filter which will not transmit particles of microscopic size and yet will allow the virus of a certain disease to pass into the filtrate, we can not expect to see the individual entities in the virus.

Several factors influence the filterability of a virus, namely, the kind of filter used, the character of the menstruum in which the virus is suspended, the degree of pressure or vacuum used, the amount of time allowed to the process, the temperature, the motility of the particles, and other factors. Unfortunately, in the study of the literature of the various filterable viruses we sometimes fail to find exact data on all these points.

Peripneumonia.—Peripneumonia^a of cattle is the only filterable virus which has so far given a visible growth on artificial media. Collodion sacs were filled with Martin's peptone bouillon, to which was added a little serum of the rabbit or cow in the proportion of 1:20. The sac was then inoculated with peripneumonia and placed in the peritoneal cavity of rabbits and cows for fifteen to twenty days. The fluid became turbid and in it, under a magnification of 2,000 diameters, could be seen the most extremely small, moving, strongly refractile points. In a series of subcultures made from such a growth the last of the series was virulent.

The colonies on agar mixed with bouillon-serum, were transparent; small, and made up of exceedingly fine particles whose form it was impossible to determine. The microbe of this disease was made to pass the Berkefeld and Chamberland F filters, but when an albuminous diluting liquid was used, it could not be made to pass either.^b

Foot-and-mouth disease.—Loeffler and Frosch^c state that lymph was taken from the blebs of calves suffering with this affection, diluted with 35 parts of water, and then passed through a filter candle. The filtrate, in amounts which correspond to one-tenth to one-fortieth cubic centimeter of the original lymph, when injected into calves caused them to sicken in two days, the same as the control animals into which were injected equal amounts of unfiltered fluid.

McFadyean says that foot-and-mouth disease passes the Berkefeld filter when in watery suspension, but is arrested when in an albuminous fluid.

Nocard^d says that aphthous fever passes through Berkefeld, Chamberland, and Kitasato filters.

South African horse sickness.—Nocard^e succeeded in passing the virus of this disease through a Berkefeld filter only.

McFadyean^f reports that pure blood taken from an animal sick with the disease was passed through the Berkefeld filter under a pressure of 26 inches of mercury and the filtrate, when inoculated into a horse, produced the disease.

When the blood serum was diluted with four parts of water and

^a Nocard, Roux, Borrel, Salimbeni et Dujardin-Beaumetz: Le microbe de la peripneumonie. Ann. de l'Inst. Pasteur, vol. 12, 1898, p. 240, etc.

^b Nocard, Roux, and Dujardin-Beaumetz: Etudes sur la peripneumonie. Recueil de med. vet., 1899, 8e. serie, Oct. 26, 1899, p. 441.

^c Loeffler and Frosch: Bericht der kommission zur erforschung der maul und klauenseuche bei dem Inst. f. Infek.-krank. in Berlin. Centbl. f. bakt. u. infek., 1898, bd. 23.

^d Nocard: La "horse sickness" ou "maladie des chevaux de l'Afrique du Sud. Bull. de le soc. centr. de med. vet., n. s., vol. 19, 1901, p. 37.

^e Journ. comp. path. and therap., 1900, XIII.

filtered through a Chamberland B filter for two hours under a pressure of 29 inches of mercury, the filtrate was infective to a horse into which it was injected. After an incubation of three days and a clinical course of six days the horse died.

Exudative typhus of chickens.—Magiora and Valenti^a made experiments with the emulsions of the blood, lungs, liver, spleen, kidneys, and heart. They used the Berkefeld filter and Chamberland F. Dilutions were made with 40 and 60 parts of physiological salt solution and a pressure of $1\frac{1}{2}$ atmospheres was employed.

Bacteriological examination of the filtrate proved negative, but chickens injected with 5 cc. of the filtrate died in about two days, presenting the same clinical and pathological picture as the naturally infected ones.

Another set of chickens injected with the blood of the ones which had received the filtrate developed typical symptoms and post-mortem changes of the disease.

An exposure of five minutes at 65° C. sterilizes the virus.

These investigators found that the filtrates had very much less virulence than the unaltered blood. Four cubic centimeters were found to represent the minimum fatal dose of a filtrate from a mixture of blood and water in the proportion of 1:160, whereas 4 cc. represented the minimum fatal dose of an unfiltered mixture of blood and water in the proportion of 1:1,500,000.

It is interesting to note how the filtration experiments cleared up an error which former students had made in regard to the loss of virulence in pure cultures of organisms which they had isolated in this disease. They had found a *cocco bacillus* in the internal organs. The culture tubes inoculated from the body fluids showed growths of this organism. Inoculations into chickens from colonies on the first set of cultures caused the disease, but subcultures from the first set of cultures were not virulent. Into the first set of cultures there had evidently been carried some of the invisible virus along with the *cocco bacillus*.

Mosaic disease of the tobacco leaf.—Beijerinck^b pressed the sap out of diseased plants and passed it through very thick porcelain filters, and the filtrate was free from bacteria, but virulent for the tobacco leaf.

Epithelioma contagiosum of fowls.—It was found by Marx and Sticker^c that the infective agent suspended in sodium chlorid solution passed through a Berkefeld filter, but not through a porcelain filter. The filtrate gave no growth on media; it was carried through a series

^a Magiora and Valenti: Ueber eine seuche von exsudativen typhus bei hühnern. Zeit. für hyg. und infekkr., vol. 42, 1903, p. 198.

^b Centrbl. für bakt., Abt. 2, bd. 5, 1899, p. 27.

^c Deut. med. wochenschr., bd. 28, 1902, p. 892.

of 16 generations in fowls; it resisted 60° C. for three hours, and after one hour in a vacuum tube at 100° C. it was virulent.

Hydrophobia.—Remlinger and Riffat-Bey^a ground up a rabbit's brain in water together with a bouillon culture of chicken cholera and filtered it by aspiration through a Berkefeld V filter. The filtrate inoculated into rabbits caused rabies.

Celli and de Blasi^b ground the brain and spinal cord in sand under 300 atmospheres pressure. A suspension in distilled water, when subjected to a small Berkefeld filter under a vacuum of 570 mm. for half an hour, gave an infective filtrate.

Remlinger (Ann. de l'Institut Pasteur, v. 17, No. 12, 1903, p. 834) confirmed his earlier work with Riffat-Bey mentioned above. He showed that the virus of hydrophobia can not be made to pass through a Chamberland filter nor through a Berkefeld N or W. It can only be forced through a Berkefeld V, which filter is the most porous of the Berkefeld system.

Hog cholera.—De Schweinitz,^c in a preliminary note, mentions a disease peculiar to hogs, indistinguishable clinically and at post-mortem from hog cholera, but which can be transferred from hog to hog by inoculation with certain body fluids which have been rendered free from bacteria by filtration through the finest porcelain filters. This filtrate was shown to contain no organisms of hog cholera or swine plague, because when inoculated into rabbits and guinea pigs the animals remained healthy.

Rinderpest.—Nicolle and Adil-Bey^d passed the virus of this disease through a Berkefeld filter, but not through a Chamberland F.

Clavelee (sheep pox).—Borrel^e filtered a suspension of the pustules in water. The filtrate from the Berkefeld filter was infective, but that from the Chamberland F was not.

Nonfilterability of vaccine and smallpox.—Parke^f crushed vaccine virus with fine sand, using 25 tons of pressure to the square inch. One portion of the suspension of crushed virus was passed through a Berkefeld filter and another portion through a Chamberland filter. Both filtrates were evaporated over sulphuric acid in a vacuum.

Calves and rabbits inoculated with the filtrate before and after

^a Remlinger and Riffat-Bey: Le virus rabique traverse la bougie Berkefeld. Compt. rend. heb. des Sec. de la Soc. de Biol., vol. 55, 1903, p. 730.

^b Deut. med. wochenschr., vol. 29, p. 945.

^c U. S. Dept. of Agriculture, Bur. Animal Industry, Circular No. 41, Sept., 1903.

^d Nicolle et Adil-Bey: Études sur la peste bovine. Ann. de l'Inst. Pasteur, vol. 16, 1902, p. 56.

^e Borrel: Experience sur la filtration du virus claveleux. Compt. rend., Soc. de Biol., vol. 54, 1902.

^f Assn. Am. Physicians: Trans., vol. 17, 1902.

evaporation failed to show any reaction. Control animals inoculated with the crushed material before filtration always had successful vaccinations. The object of the crushing was to liberate the organisms from epithelial cells or other tissues which might retain them.

Smallpox virus from three fatal cases failed after crushing to pass into the filtrate, as determined by the inoculation of monkeys.

Filterable bacteria.—Von Esmarch^a sought to determine whether there are such things as ultramicroscopic organisms among the saprophytes.

We readily believe that the virus of a filterable infectious disease is made of very small organisms, possibly ultramicroscopic, and that if these organisms could be made to multiply the resulting mass would have an appreciable size. If there are ultramicroscopic saprophytes he thought that all conditions were in the highest degree favorable for their multiplication, and that on the ordinary laboratory media they ought to find their most suitable conditions of growth and give an appreciable evidence of their existence.

He used 40 different kinds of fluids, including sewage, rich vegetable infusions, decomposing urine, emulsions of sputum, cavadars, and feces. The clear filtrates from these suspensions were planted on all the laboratory media and these plants kept under different conditions showed no growth.

During the first week's observations of the original filtrate no growth was noted; but after ten days this fluid showed a turbidity which was due to a very fine motile organism (*Spirillum parvum*), which grew as vibrios and spirilla, which were recognized only by the greatest magnification. It passed the Berkefeld, Chamberland F, Reischel, and Pukall filters and appeared in the first 200–300 cc. of filtrates. No other bacteria were found in the filtrates. Its size is about the same as that of the influenza bacillus, being 1 to 3 micra in length and 0.1 to 0.3 micra in width.

Von Esmarch grew bacteria through filters which hold them back in ordinary filtration work. He used Berkefeld, Kitasato, and Maassen filters.

These filters were filled with plain bouillon and were placed in a vessel containing bouillon inoculated with an organism, and the whole was kept at 37°, or room temperature.

Typhoid grew through the Kitasato filter at 37° in twenty-four hours, and at room temperature in two days.

Cholera went through a Maassen filter at 37° in two days, but a control kept at room temperature did not grow through after thirteen days.

A small Berkefeld filter allowed *Bacillus prodigiosus* to pass in

^a Centbl. fur bakt., bd. 32, 1902, p. 561.

from one to three days, and a large Berkefeld allowed *pyocyaneus* and *prodigiosus* to pass in seven days.

Wherry^a states that the bacillus producing pneumonia in guinea pigs (0.5 micron wide and 0.7 micron in length) passed the small Berkefeld No. 5, but was not found in the filtrate from the thicker walled Berkefeld No. 8, nor in the filtrate from the Chamberland F. It, however, grew through the walls of all three.

FOMITES.

While we made no experiments directly designed to determine the part played by fomites in transmitting the infection of yellow fever, still our work strongly bears on this point, and we can fully corroborate the conclusions of Reed and Carroll that fomites or inanimate objects are not dangerous in this respect.

Nonimmunes whom we kept for weeks under observation in our mosquito-proof rooms slept on the same beds, used the same clothing, washed from the same bowl, ate the same food, drank the same water, and breathed the same air as those sick with yellow fever; nevertheless they remained free of all fever except that which was purposely given them by mosquito bites or blood inoculations.

As these experiments were done in the summer time at Vera Cruz, a badly infected city where the disease prevailed at the time in epidemic form, it removes some of the objections which were made at the time to the work of the Army Commission, which for the most part was done during the winter months in an otherwise healthful locality—Camp Lazear.

THE FILTRATION OF MALARIAL BLOOD.

The filtration experiments with malaria were undertaken with the hope that they would throw light upon yellow fever, which bears so many analogies to malaria. Both diseases are transmitted by mosquitoes, and it is therefore natural to suppose that yellow fever is due to an animal parasite, perhaps similar to the well-known plasmodium of Laveran. However, as the one disease is filterable and the other is not; and as the parasite of the one is visible and the other can not be seen with the highest powers of the microscope at present at our command, either in the mosquito or in man; and as the one produces an immunity and the other does not, we find the analogy is not after all so very striking and that it does not seem helpful in solving our problem.

The malarial rosette breaks and liberates spores (*merozoites*) which are exceedingly minute, and in order to carry out the analogy in an

^a Journ. med. research, vol. 8, 1902, p. 322.

experimental way we filtered malarial blood in order to determine whether there might be forms of the malarial parasite which are even smaller than this spore.

We know from the work of Novy that a trypanosome (*Trypanosoma Lewisi*), which is a colossal organism when compared with a malarial spore, has forms which are so minute that they pass a Berkefeld filter, for he has succeeded not only in artificially cultivating the adult trypanosome parasite, but in infecting animals with the filtrate from these cultures. We also know from the recent work of Schaudinn^a that some of the animal parasites (*Spirochaeta*), multiply by reducing division; that is, each time cleavage takes place the organism is reduced in size, and this process continues until the divided forms become too small to be seen as individuals and can be made out only as clusters.

We therefore reasoned that if the malarial parasite has an ultra-microscopic form minute enough to pass the pores of a filter, it would encourage us very much to look for a visible form of the yellow fever organism in the blood and tissues of man and the mosquito by the aid of technique that had not previously been employed.

Our filtration experiments with malarial blood resulted negatively so far as demonstrating the presence of a minute or ultramicroscopic form of this parasite was concerned, but there developed unexpectedly what appears to be a demonstration of the malarial toxin. We produced a definite paroxysm by the inoculation of blood serum freed of the malarial parasites by filtration; and it is reasonable to suppose that the same substance circulating in the blood, which caused the chill, fever, and sweat in one man, caused a precisely similar chain of symptoms in the other two into whom this serum was transferred.

We found that if the blood is drawn after the height of the paroxysm and while the fever is declining this poison is not manifest; but if the blood is taken during the chill and while the temperature is rising, it is present.

If this poison is the toxin causing a malarial paroxysm it is remarkable that it should be present in the blood serum in such a considerable quantity and disappear so very rapidly. Still, the clinical symptoms of the disease would indicate the sudden production of a large quantity of toxin and its rapid elimination, neutralization, or destruction. So far as we know, this is the first time that a poison has been demonstrated which is capable of reproducing the symptoms of a disease due to an animal parasite of microscopic size.

It would be folly from a few observations to claim that we have discovered the malarial toxin. The only conclusion justified is that we have demonstrated the existence of some poison in the blood which is

^a Loc. cit.

capable of reproducing the symptoms of the disease when injected into the veins of other men.

We are not unmindful of the fact that chemical substances derived from the hemoglobulin or other proteids in the blood may be toxic, and we are of course familiar with the work of Gauldi, Montesano, Mannaberg, Celli, and others, who failed to demonstrate a pyrogenic toxin in malarial blood from similar experiments. The length of time the blood was exposed to the air between the time it was drawn from the malarial patient until it was injected into the person experimented upon may account for the discrepancies in results. The time the blood is drawn in relation to the paroxysm and many other factors should also be taken into account.

Mannaberg^a drew blood during the attack in a case of ordinary tertian malaria. He centrifugalized it and injected the clear serum subcutaneously into two healthy people.

One received 1 cc. of serum at 4 p. m., when his temperature was 36.7° C. The temperature at 4.30 p. m. was 37° and at 6 o'clock 36°.

The other patient was given 0.7 cc. of the serum and his temperature rose within fifteen minutes after the injection from 36.5° to 37.6° C.

Celli^b took during the cold stage a small quantity of blood from each of many malarial patients.

Young children were inoculated with 50 cc. of the serum subcutaneously and 50 cc. intravenously.

Another child was given the concentrated serum remaining after treating 260 cc. of serum in a vacuum apparatus at low temperature. The child was injected intravenously and subcutaneously.

From a hemorrhage in a case of severe comatose pernicious malaria 25 cc. of serum were obtained and injected into another patient.

None of the patients into whom the serum was injected showed pyrexia. There was in several instances, however, a slight rise of temperature which the experimenter says may occur after the injection of normal serum.

Rievel and Behrens^c studied a sarcosporidium of the llama. They removed ten of the sacks and ground them up with physiological salt solution in a mortar, and injected 2 cc. of the fluid subcutaneously into a rabbit. After seven hours the rabbit died. The autopsy revealed nothing unusual.

^a Mannaberg, Julius: Die malaria krankheiten. Nothnagel's Specielle Pathologie und Therapie, Bd. 2, 1899.

^b Celli, Angelo: Malaria. Transl. by J. J. Eyre. Longmans, Green & Co., New York and London, 1900.

^c Rievel and Behrens: Beiträge zur Kenntnis der Sarcosporidien und deren Enzyme. Centralblatt für bakt. u. parasit. (orig.). Bd. 35, no. 3, s. 341.

Another rabbit received by mouth the contents of several sacks rubbed up in salt solution. This rabbit was given at the same time a subcutaneous injection of 1 cc. of the fluid. The animal died after eight hours. From a gross examination of his internal organs and a bacteriologic examination of the same, nothing abnormal was found.

Blood from the spleens of the above-mentioned rabbits, when injected into three other rabbits, caused no abnormal symptoms.

Pieces of the flesh of the llama were cut up in salt solution and the fluid part was injected into two rabbits subcutaneously. Both remained sound.

A rabbit inoculated subcutaneously with a suspension of the contents of sarcosporidia sacks in salt solution died after seven hours. The post-mortem was negative.

Two other rabbits treated in the same way remained alive six hours. Another died after seven hours.

A suspension was subjected to dialysis and it was found that the dialysat, when injected into a rabbit, caused death within twenty-four hours. The cooked dialysat was inactive.

Our experimental cases in malaria follow:

FILTRATION EXPERIMENTS WITH ESTIVO-AUTUMNAL FEVER.

Filomena Martinez (case LXIII), 35 years old, born in Mexico City, lived in Vera Cruz about one year.

The patient was admitted to the hospital of Working Party No. 2 October 27, at 10 a. m. He had been under observation the previous day and early that same morning at San Sebastian Hospital.

As he showed a heavy infection with malarial parasites he was transferred to our laboratory.

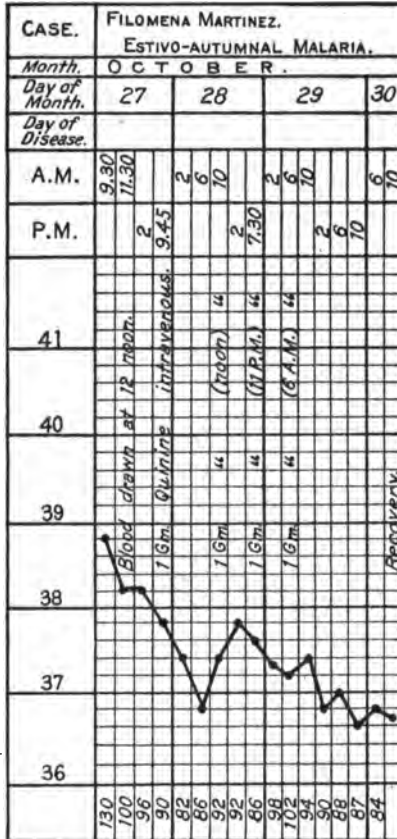
He gives a history of having had yellow fever about six months ago. His present illness, according to his statement, began some two weeks ago with fever, but he says he did not have chills. The patient's mental condition when seen was below par, and he was unable to give consistent answers. He seemed somnolent and was evidently beginning to show the effects of his infection upon the brain.

An examination of his blood, taken at 4.15 p. m., October 26, showed very many young ring forms, some of them with active amoeboid shapes. None appeared pigmented in the smears stained with Goldhorn's polychrome methylene blue. Crescents and ovoids also present.

At 12 o'clock noon, October 27, a trifling incision was made through the skin over the median cephalic vein on the right side. A needle was introduced into the vein and 100 cc. of blood were quickly drawn into a sterile flask. The wound was covered with a sterile dressing and healed without complications.

The blood was immediately put into the ice chest, the temperature of which registered between 16° and 19° C. Clotting took place rapidly. The red cells settled to the bottom of the flask, the upper part of the clot being composed of a firm yellowish buffy coat. The serum separated well and was very clear.

The blood serum was drawn off and diluted with an equal volume of an isotonic salt solution and then divided into two portions.



One portion was passed through a Chamberland B filter and injected into José Ojeira.

The other portion was passed through a Berkefeld filter and injected into Luis Peredo.

Blood smears made from the blood which was drawn from the vein showed in stained specimens crescents and the young small ring forms of estivo-autumnal malaria. Some of the stained parasites showed one chromatin point, others two. A few were irregular in outline,

EXPLANATION OF PLATE 2.

Estivo-autumnal malaria.

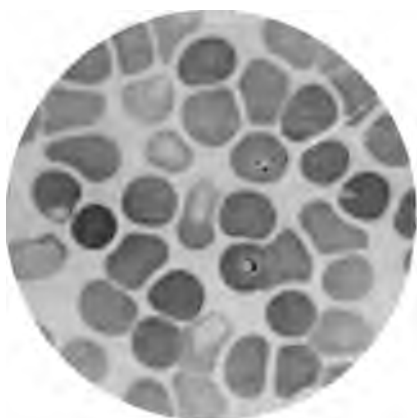
The character of the malarial parasites in the blood of Flomena Martinez at the time it was filtered.

Stained with Goldhorn's polychrome methylene blue.

1. Small ring forms.

2. Young ameboid forms.

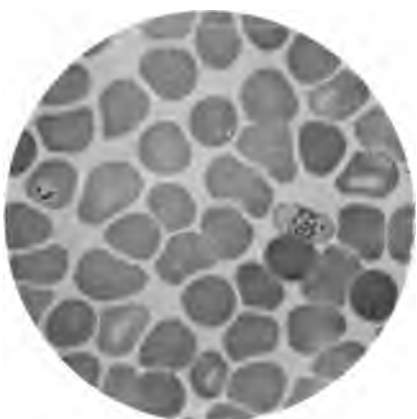
3, 4, 5, and 6. Ovoids.



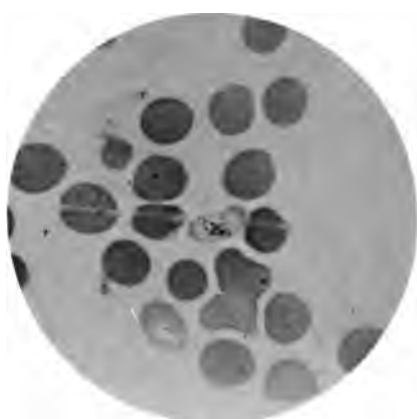
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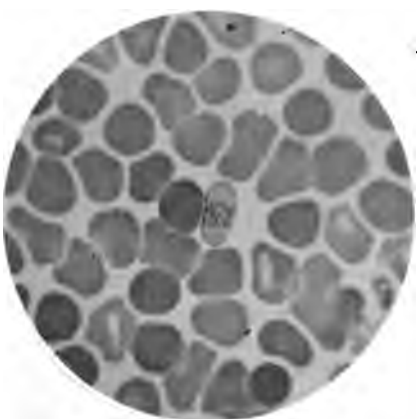
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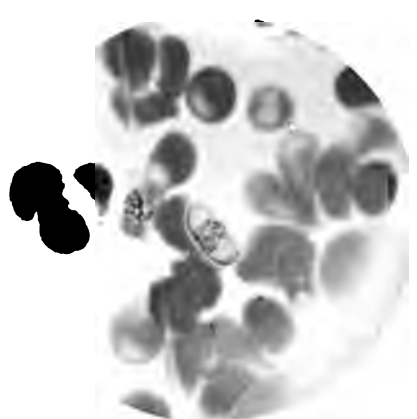
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4



5



6

CHARACTER OF THE MALARIAL PARASITES IN THE BLOOD OF FILOMENA MARTINEZ
AT THE TIME IT WAS FILTERED.

indicating older parasites with amœboid motion. These latter were two or three times the size of the small ring forms. (See plate 2.)

These irregularly shaped parasites had two and some three chromatin points. In the blood taken at subsequent periods similar forms were seen, the older or younger forms predominating, depending upon the time of day the blood was examined.

The details of diluting and filtering the blood serum of Filomena Martinez follow:

At 5.30 p. m. the blood was taken from the ice chest, having been there just five and one-half hours, and 27 cc. of the clear serum were pipetted off. This serum contained a few flakes and very few red blood cells.

To this serum was added an equal amount (27 cc.) of physiological salt solution (0.6 per cent).

The mixture was transferred to a filter flask and a Chamberland B filter was carefully lowered into the fluid and securely fastened in position. This was a new filter marked as follows: "B. filtre Chamberland système Pasteur H. B. Cie., Choisy-le-Roi. BTE S. 6.O.G. Contrôlé."

The filter was tested before using with an air pressure of 30 pounds, after which it was lowered into water. When first lowered into the water the air came from every part of the surface of the filter in very fine bubbles, but nowhere was there evidence of a crack or pinhole. As soon as the filter became wet no air could be forced through it with a pressure of 30 pounds. This particular candle was considered to be tighter than the other Chamberland-Pasteur filters which we had similarly tested.

The filter was then thoroughly washed by allowing 200 cc. of water to pass through it under 20 pounds pressure. It was sterilized in the hot air sterilizer for one hour on the day before the blood was filtered, at a temperature of 150° C. for one hour.

The filtration was begun at 6 p. m., October 27, and was conducted in accordance with the diagram (fig. 2) by means of pressure from an air pump. This air pump was worked by hand and the diluted blood serum filtered under a pressure of 15 pounds. The pressure was controlled by the gauge, as shown in the sketch.

Very slight variations occurred both above and below 15 pounds, owing to the difficulty of exact control with hand power.

The pressure was kept up for one hour, and the filtrate was drawn from the inside of the bougie with a long sterilized pipette. In this manner it will be noticed that there was no possible chance of contact between the filtrate and the blood serum, and throughout the process the greatest care was taken in order to prevent such a contamination. The filtrate as it came through the filter was clear and of amber color.

At 7.20 p. m. 20 cc. of the filtrate were injected by means of an appropriate syringe with hypodermic needle into the left median cephalic vein of José Ojeira with entirely negative results.

A second portion of the blood serum of Filomena Martinez was

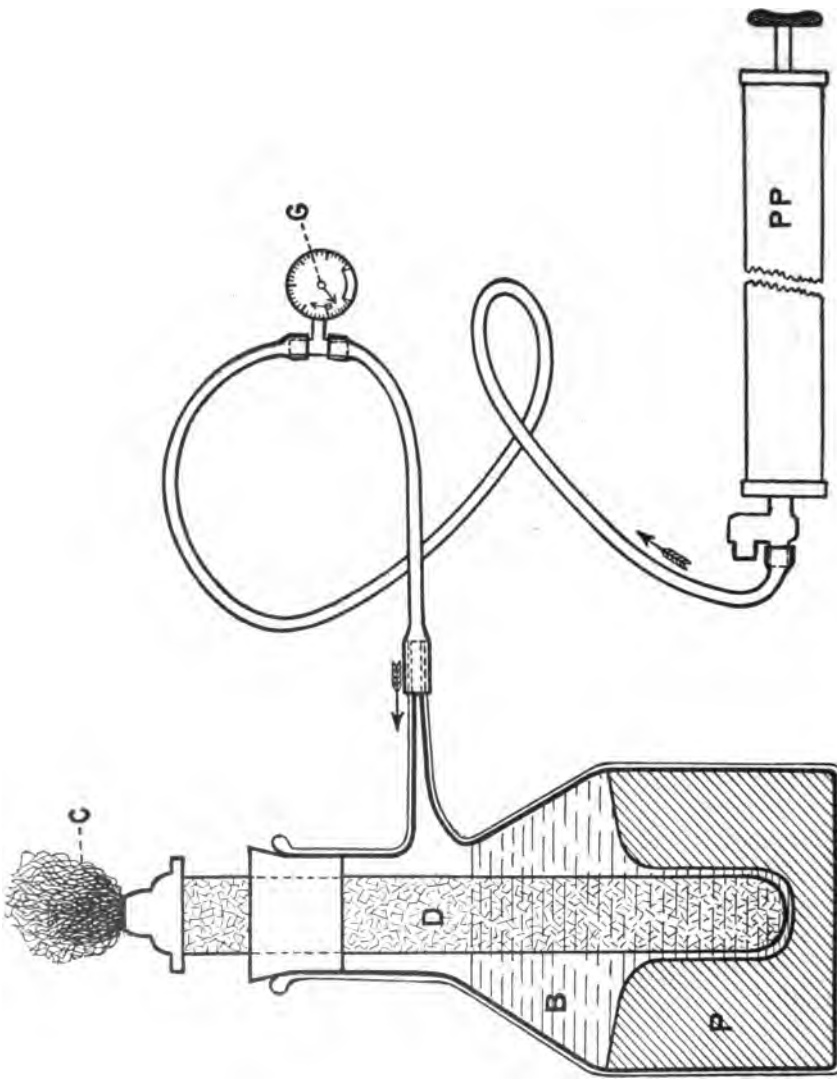


FIG. 2.—The arrangement used for filtering through a Pasteur-Chamberland bougie B. PP, pressure pump. G, pressure gauge. D, Pasteur-Chamberland bougie, stopped with cotton and sterilized; held in place by a rubber stopper. P, a molded cup of paraffin to keep the small quantity of blood in contact with the surface of the filter. B, the blood serum.

pipetted off and diluted with an equal quantity of physiological salt solution, and filtered through a small Berkefeld filter, as follows:

A new Berkefeld filter was prepared by thoroughly washing by allowing water to pass through it for several hours, and then sterilized in dry heat.

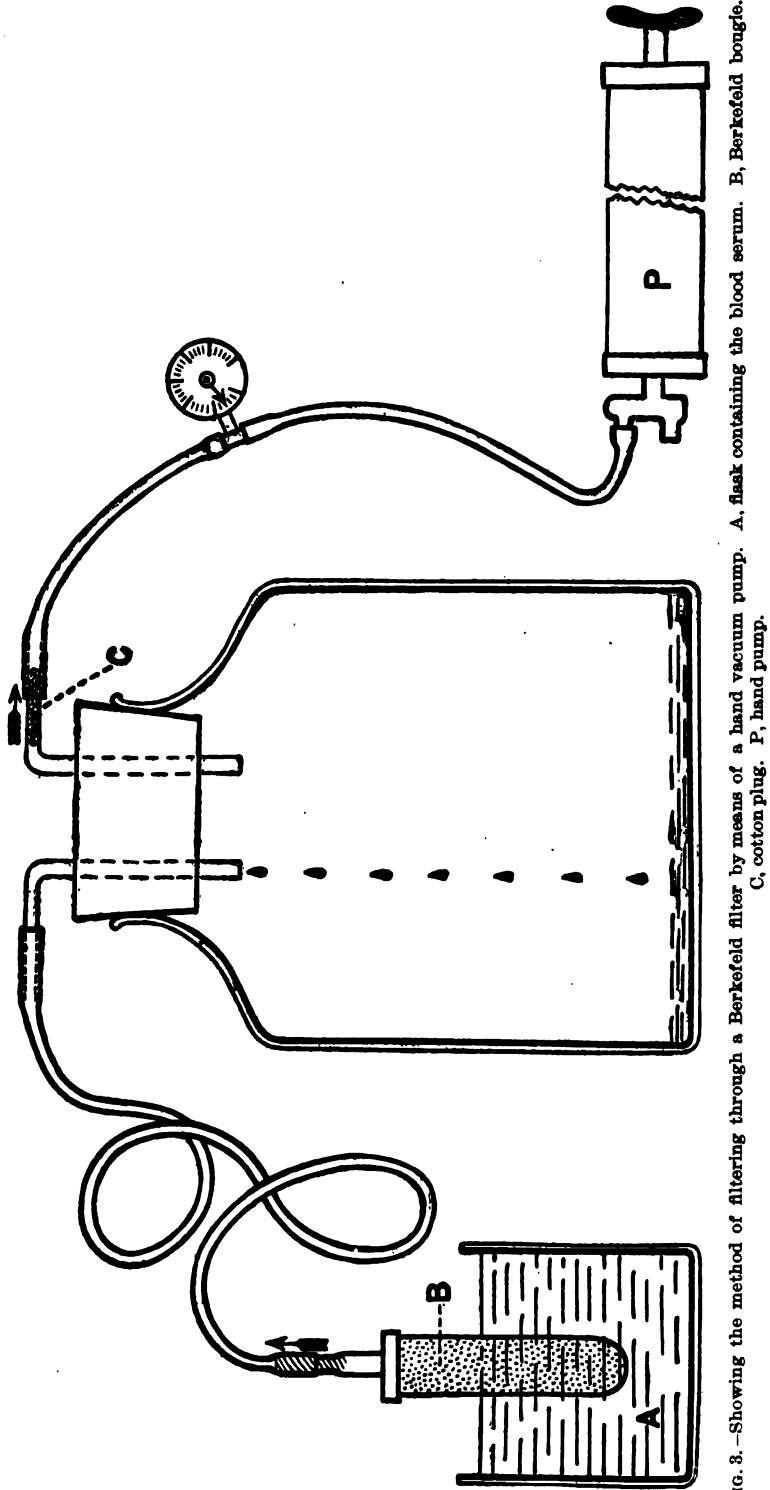


FIG. 3. —Showing the method of filtering through a Berkefeld filter by means of a hand vacuum pump. A, flask containing the blood serum. B, Berkefeld bongle. C, cotton plug. P, hand pump.

This filtration was also done from without inwards, as may be seen by reference to the sketch (fig. 3), but by using vacuum instead of direct air pressure, as in the case of the filtration through the Pasteur-Chamberland bougie. The filtrate was carried over to a sterile bottle, as shown in the sketch, and drawn out with a pipette, so that, care being taken, there could be no chance of contamination. It required about twenty minutes to filter 46.5 cc. of diluted serum, and at 8.15 p. m., viz, eight and one-fourth hours after the blood was drawn, twenty cubic centimeters of this filtrate, which represented 10 cc. of the original serum, were injected into the left median basilic vein of Luis Peredo with entirely negative results.

This filter was then thoroughly washed with water which ran through in drops under atmospheric pressure, and was preserved for further testing, with the following results:

On March 1, 1904, this filter was tested with a bouillon culture of *Staphylococcus pyogenes aureus*. The filtrate remained sterile after ten days in the incubator.

At 10 p. m. Martinez was given 1 gram of bimuriate of quinine directly into one of the veins of his arm. This was repeated at noon on October 28, and again at 11 p. m. on the same day.

On the 29th he received another gram into the vein, with marked improvement in his symptoms and a notable reduction in the number of intracorpuseular forms in the blood, as will be seen by the following notes of the case:

October 27, 10 p. m.—One gram bimuriate of quinine intravenously. Blood examination, 3 crescents in one field; some fields have as many as half a dozen small ring forms.

October 28, 2 a. m.—Blood examination. Some fields have 5 and 6 small ring forms, some irregular amœboid shapes, also ovoids.

6 a. m.—Blood examination. One or two ring forms to each field; also crescents.

10 a. m.—Blood examination. About 1 organism to each field; some young ring forms; some amœboid shapes; also ovoids.

12 noon.—One gram bimuriate of quinine intravenously.

2 p. m.—Blood examination. About 1 intracorpuseular form to each field.

11 p. m.—One gram bimuriate of quinine intravenously.

October 29, 2 a. m.—Ten-minute search of a slide stained with polychrome methylene blue showed no intracorpuseular forms; crescents not diminished in numbers.

6 a. m.—Only 2 intracorpuseular rings seen; crescents in moderate numbers.

10 a. m.—Given 1 gram bimuriate of quinine into a vein. Five-minute search of a stained blood smear shows 5 ovoids and only 1 intracorpuseular ring form.

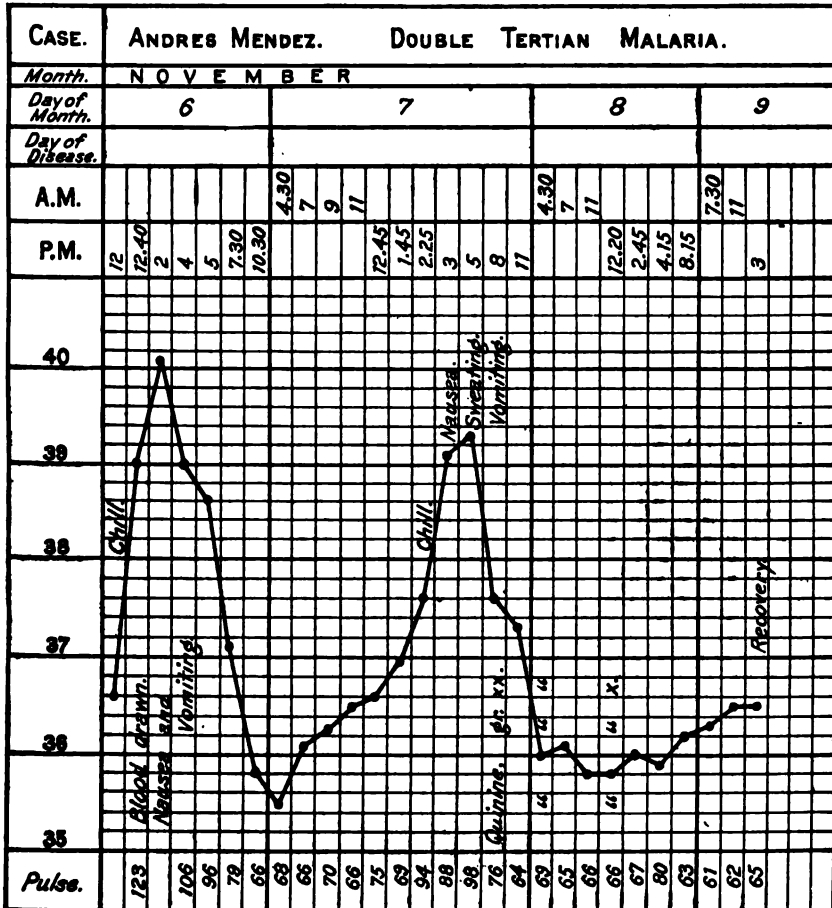
2 p. m.—No intracorpuseular forms.

10 p. m.—No intracorpuseular forms.

October 30, 6 a. m.—Blood examination shows no intracorpuseular forms. A large mononuclear leucocyte has much brown pigment. Ovoids still present in apparently undiminished numbers. Patient has very much improved in his general condition. His mind is better, appetite has returned, and he was returned to San Sebastian Hospital.

FILTRATION EXPERIMENTS WITH TERTIAN FEVER.

Andrez Mendez (case LXVI), 39 years old; born in La Luz, Estado de Guanajuato; never had fever in his native place. In 1878 had yel-



Temperature chart of Andres Mendez.

low fever (?) in San Antonio, Estado de Guanajuato, with which he says he was sick about one month. He came to Vera Cruz three years ago and has had fevers five or six times since.

Present illness dates from about November 3, but states that he has been troubled with mild attacks of fever for a month, which he describes as coming on alternate days, but not sufficiently severe to keep him from his work.

The fever which initiated his present sickness began with a severe chill, and was followed by fever and sweat, and was associated with some nausea and vomiting. He states that these paroxysms were repeated daily until his admission to San Sebastian Hospital, November 6, 1903.

Blood examination showed that he had a heavy infection with tertian parasites, and he was immediately transferred to the laboratory of Working Party No. 2, Yellow Fever Institute.

The man was physically robust, but very anemic, mucous membranes particularly pale, skin cold and damp.

At about noon on this date (November 6), the patient was seized with a chill.

By 12.30, half an hour later, the rigor was very marked; he lay in bed with a blanket drawn over his head, and was shaking violently; he could not hold a thermometer in his mouth, and the pulse was taken with difficulty. During this time the temperature was rapidly rising, it being now 39.1° C.

At 12.40 blood was drawn from one of the superficial veins at the bend of the elbow. On account of the rigor there was some difficulty in introducing the needle. The blood flowed freely; 125 cc. were quickly drawn. It was permitted to flow into a porcelain dish and immediately defibrinated by whipping with sterilized forks. Clotting took place very quickly, so that the fibrin was readily and quickly separated from the fluid.

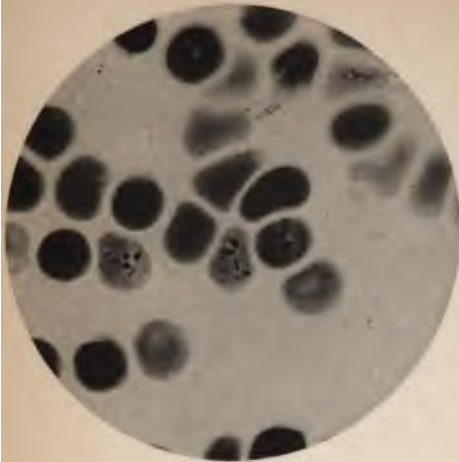
Judging from the size of the clot and color the fibrin had enmeshed a number of corpuscles. The defibrinated fluid showed no further tendency to clot, and on microscopical examination looked like fresh blood containing a normal number of corpuscles.

To 25 cc. of defibrinated blood was added 25 cc. of physiological salt solution, and this diluted blood was filtered through the same Berkefeld filter in the same manner as was done with the blood of Filomena Martinez (see p. 84). This filter, when tested later, March 1, 1904, held back *Staphylococcus pyogenes aureus*.

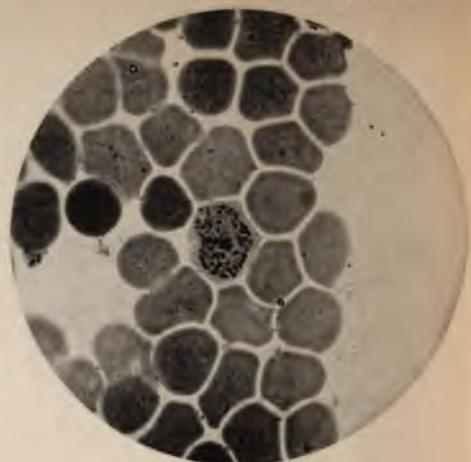
Nine cc. of the filtrate were injected into the right basilic vein of Luis Peredo as soon as this amount could be obtained. This injection took place at 1.40 p. m. It only took about forty minutes to defibrinate and filter the blood, which process was done as rapidly as possible.

Stained smears of the filtrate showed no morphologic elements. The filtrate had a distinct red color. For the method by which this filtration was done, see fig. 3.

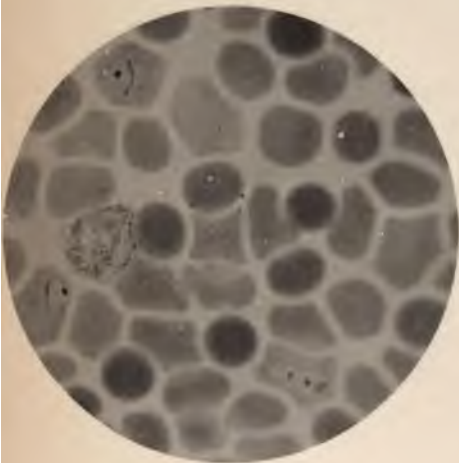
a control, José Ojeira, at 2 p. m., was given an injection into



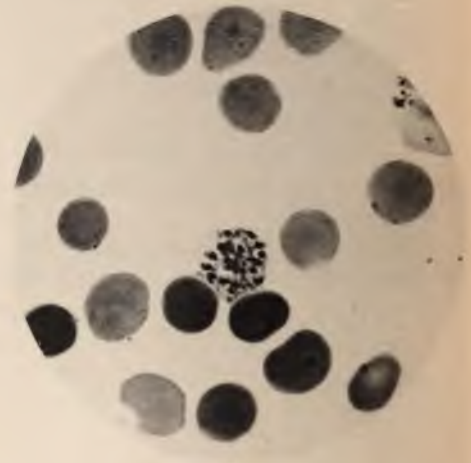
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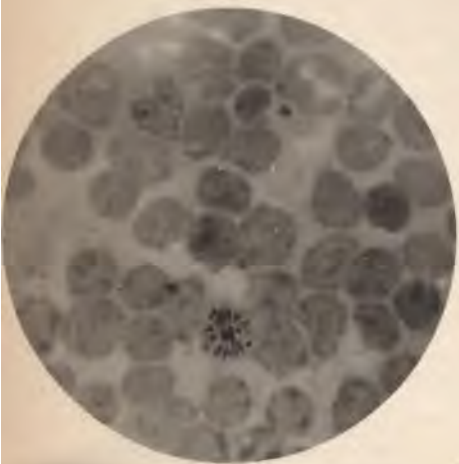
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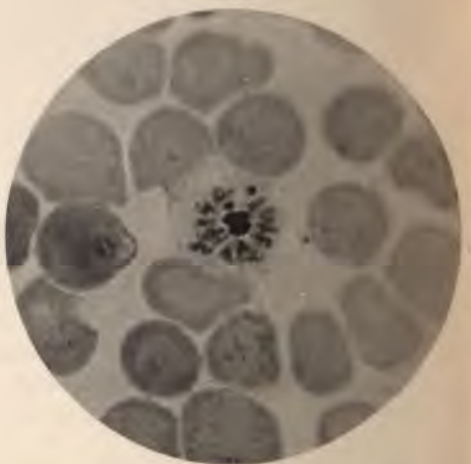
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4



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6

CHARACTER OF THE MALARIAL PARASITES IN THE BLOOD OF ANDRES MENDES
AT THE TIME IT WAS FILTERED.

EXPLANATION OF PLATE 3.

Double tertian malaria.

The character of the malarial parasites in the blood of Andres Mendez at the time it was filtered.

Stained with Goldhorn's polychrome methylene blue.

- 1. Young ameboid forms.**
- 2. Older pigmented parasite.**
- 3. Young and old forms in the same field.**
- 4, 5, and 6. Segmenting forms.**

his left basilic vein of 4 cc. of the *unfiltered* mixture. As the blood was diluted with equal parts of salt solution, he therefore received 2 cc. of Mendez's blood.

The unfiltered mixture of defibrinated blood and salt solution, upon microscopic examination shortly after Ojeira received his injection, showed amoeboid certain organisms with dancing pigment. For the character of the malarial parasites infecting the blood of Mendez, see illustration, plate 3.

After drawing the blood from Mendez he continued to have a chill, with severe rigor and chattering of the teeth, accompanied by nausea and vomiting. His temperature continued to rise after the blood was drawn until it reached 40.2° C. The febrile period was followed by drowsiness and moisture of the skin.

As will be seen by reference to the temperature chart, Mendez was kept under observation without quinine, and had another typical malarial paroxysm the next day. All the evidence in his peripheral blood, which was examined frequently, pointed to a severe double infection with the tertian parasite.

He was then given quinine, which entirely controlled the disease, and caused the complete disappearance of the parasites from his peripheral blood.

The results caused by the injection of the blood of Andres Mendez into Peredo and Ojeira follow:

Luis Peredo (case LXIV), a volunteer, aged 25, born in Jalapa, State of Vera Cruz, where he has always lived. When examined at Jalapa, August 26, he was found to be physically sound; urine contained no albumin; peripheral blood showed no plasmodium.

He was brought to Vera Cruz August 28 and taken from the station directly to the laboratory, from which time he was kept constantly within a mosquito-proof room.

On October 27, after having been under daily observation two months, during which time he remained in normal health, he was injected with the filtered blood of Filomena Martinez (page 84), who at the time was suffering with a paroxysm of malarial fever of the estivo-autumnal type, his blood containing many young ring-forms and crescents.

It will be noted by reference to the records of Filomena Martinez that the blood was drawn during the decline of the paroxysm. It was then allowed to clot in the ice chest; the clear serum was pipetted off and diluted with an equal quantity of isotonic salt solution, and this filtered through a new Berkefeld filter.

Twenty cubic centimeters of the filtrate, which on account of the dilution represented 10 cc. of the blood serum, were injected into the left median basilic vein of Peredo.

For further details of the manner in which the blood serum was obtained and the filtration performed, see the above records of Filomena Martinez.

Peredo was carefully watched from the hour he was injected, but he remained in good health, and no deviation from the normal was detected.

His temperature was taken every four hours during the night and day, both before and following the injection, as will be seen by the temperature chart. No symptoms developed.

His blood was examined daily for plasmodium, but none was found. The result of this injection must therefore be considered negative.

Ten days later he was again injected with filtered malarial blood under different circumstances, and with positive results.

At 1.40 p. m., November 6, he was given an intravenous injection of the blood of Andres Mendez, passed through the same Berkefeld filter as before. Mendez was suffering with a double tertian infection; his blood was drawn during his chill and before the height of the paroxysm, as will be seen by reference to the temperature chart (page 85).

Thinking that allowing the blood to clot four or five hours in the ice chest in order to obtain a clear serum for filtration might be too severe a tax upon the vitality of the malarial parasite, we this time defibrinated the blood as quickly as possible, diluted it as before with an equal volume of physiological salt solution, and filtered it through the same Berkefeld filter in the same manner as was done with blood of Filomena Martinez.

As soon as 9 cc. of the filtrate could be obtained it was injected into the basilic vein of the right arm of Louis Peredo. This injection took place at 1.40 p. m.

About thirty-five minutes after receiving the injection he began having chilly sensations and headaches, and presently went to bed covering himself with his blanket (2.25 p. m.). Five minutes later (2.30) he was having a violent chill, his teeth chattering so that we could not trust the thermometer in his mouth. The rigor of the entire body was so marked that there was difficulty in taking the radial pulse. The face was pale, and at this time he vomited most of the dinner he had eaten a short time before receiving the injection.

The patient complained of headache, which he localized at the forehead and occiput; says he felt cold and had pains in the knees. At this time the skin was dry. The chill lasted somewhat over half an hour.

At 3 p. m. the patient had transient chilly creeps, very slight rigor.

At 3.15 p. m. he said he felt "warm inside," and all sense of chilliness had disappeared; still has headache.

At 3.25 p. m. he complained of marked pain in the legs.

At 3.30 p. m. vomited the remainder of his dinner.

It will be seen from the temperature chart that during this time his temperature was rapidly rising and reached its highest point (38.7° C.) at 4 o'clock p. m., just two hours and twenty minutes after receiving the injection.

The pains in the knees and back continued, and nausea and vomiting now became a distressing feature of the paroxysms for the patient.

The fever gradually subsided, and reached normal at 4.30 a. m. that same night. (See temperature chart.)

As the fever subsided the skin became moist, the nausea and pains gradually disappeared, so that by 6 o'clock p. m. the patient was quiet and dozing. The entire paroxysm, therefore, according to the temperature record, lasted about eight hours, although the patient was sleeping quietly five hours after receiving the injection.

It is interesting to note that this man Peredo had what seemed to be a typical malarial paroxysm beginning with a distinct rigor associated with a rise of temperature and followed by slight sweating. It is of particular interest to note that his paroxysm, so far as symptoms were concerned, was very much like the paroxysm from which Andres Mendez suffered, especially the nausea and vomiting.

Peredo was kept under very close scrutiny until November 24, eighteen days following the injection, during which time he remained entirely normal and no plasmodium appeared in his peripheral blood, which was frequently examined, as follows:

Blood examination.—Goldhorn's stain.

November 6.—4.30 p. m., 8 p. m. No malaria.

November 7.—4.30 a. m., 8.30 a. m., 12.30 p. m., 5 p. m., 11 p. m. No malaria.

November 8.—7 a. m., 1 p. m., 6 p. m., 9.30 p. m. No malaria.

November 9.—7.30 a. m., 1.30 p. m. No malaria.

November 10.—2 a. m., 3.30 p. m., 8 p. m., five minutes each. No malaria.

November 11.—4, 7, 10 a. m., 2, 6, 11 p. m., five minutes each. No malaria.

November 12.—1.30, 6.25 a. m., five minutes each. No malaria.

November 13.—7 a. m., 9.30 p. m., five minutes each. No malaria.

November 14.—8 a. m., 8 p. m., five minutes each. No malaria.

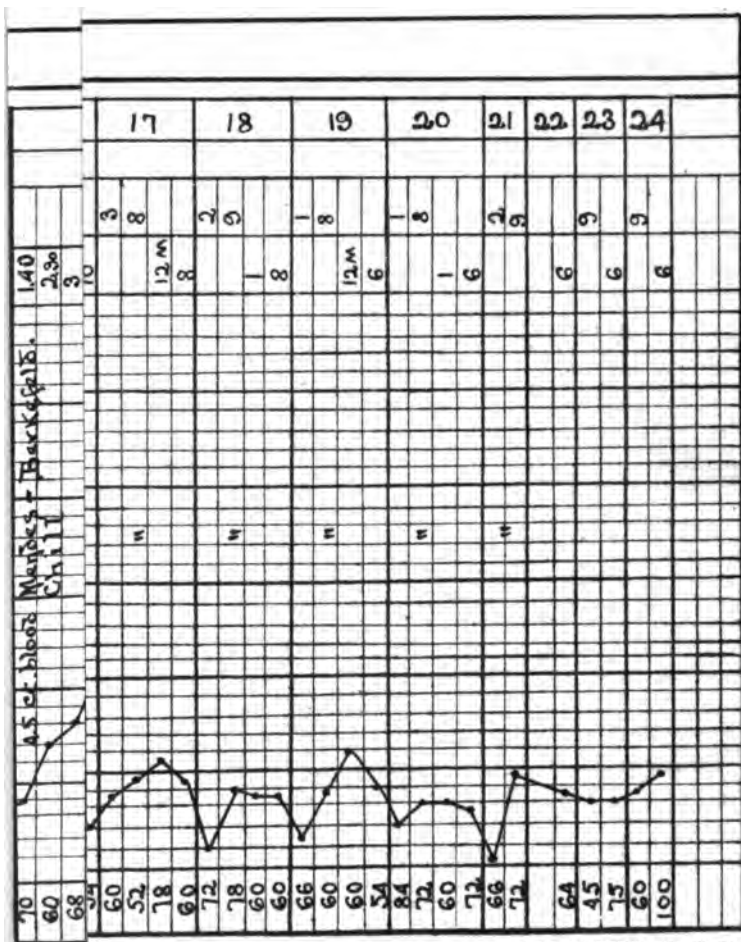
November 15.—8 a. m., 8.30 p. m., five minutes each. No malaria.

November 16.—7 a. m., 9.30 p. m., five minutes each. No malaria.

November 17.—8 a. m., 8 p. m., five minutes each. No malaria.

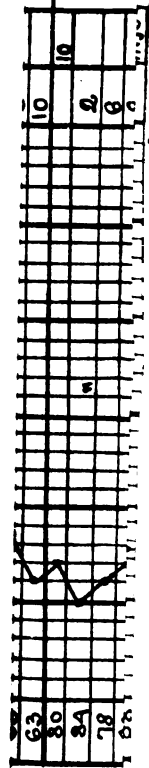
José Ojeira (case XXIII), a volunteer from Jalapa, 18 years old; had never lived on the coast, and says he never had fever of any kind. On examination in Jalapa, August 11, he was found to be physically sound, of robust physique; urine showed no albumin, and blood examination for malaria was negative.

He was taken to Vera Cruz August 13, and immediately transferred to a mosquito-proof room in the laboratory, where he was kept under close observation.



ARIA.

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On August 28, at 9.30 a. m., he was bitten by four mosquitoes, two of which had bitten Antonio Leal (case XXXV), a yellow-fever patient ten days seventeen hours previously; and the other two had bitten the same case fourteen days twenty-three hours previously.

The man was kept under close observation in a mosquito-proof room, but showed no reaction. There was no rise of temperature, nor did he present any untoward symptoms.

On October 27, 7.20 p. m., he received intravenously 20 cc. of diluted blood serum of Filomena Martinez (æstivo-autumnal infection), passed through a Pasteur-Chamberland filter B. This represented 10 cc. of blood serum. For details of this filtration see Filomena Martinez (p. 81).

Ojeira showed no reaction whatever as a result of this injection.

It will be noted that the blood of Martinez was drawn after the height of the paroxysm, and while the temperature was on the decline. Martinez was suffering with a very severe æstivo-autumnal infection at the time the blood was taken.

Ojeira's blood was carefully examined several times daily, both before and following this experiment, and at no time was anything resembling a malarial parasite seen in his peripheral blood.

On November 6, the patient having continued in good health since the last experiment, was used as a control for the experiment made on Peredo.

On this date, at 2 p. m., he was given an intravenous injection of 4 cc. of the *unfiltered*, diluted, and defibrinated blood of Andres Mendez. At the time the blood was drawn from Mendez it contained a heavy infection of a double tertian malaria, and the blood was taken from him during a chill and before the height of his paroxysm. It was at once defibrinated, diluted with an equal volume of physiological salt solution, and filtered through a Berkefeld filter. Nine cc. of the filtrate were given intravenously to Peredo, causing a malarial paroxysm without, however, the presence of the malarial parasite, and due, as we believe, to the toxin (?) in the blood of Mendez.

Ojeira, who received 2 cc. of unfiltered blood (4 cc. dilution), reacted within an hour, with a slight rise of temperature and nausea, and four days following developed a typical malarial paroxysm, with many tertian parasites in his peripheral blood.

There can be no doubt that the reaction to the 2 cc. of defibrinated blood injected into the vein of Ojeira caused a slight paroxysm, which it is reasonable to suppose was due to the same poison present in the blood of Mendez, and which also caused the reaction in Peredo.

It will be noticed that 2 cc. of this blood caused but a slight reaction in the case of Ojeira, while 4.5 cc. caused a more marked reaction, with a rise of temperature to 38.7° C., in the case of Peredo,

indicating in a very definite manner that the severity of the symptoms were directly due to the quantity of poison introduced. Ojeira did not have a chill or other manifestations of a malarial paroxysm, other than a rise of temperature and nausea. He vomited gastric mucus several times.

On November 10, the fourth day following the injection, Ojeira had a typical malarial paroxysm, with tertian parasites in his peripheral blood. He suffered with a double infection, having a chill every day, as will be noticed by reference to the temperature chart.

The character of the parasites in his blood and the clinical course of the disease resembled in all respects those of Mendez, from whom the blood was taken. Both cases were entirely controlled by quinine.

MISCELLANEOUS OBSERVATIONS ON MOSQUITOES.

In association with Doctor Goldberger we made some miscellaneous observations upon the life history and biology of the *Stegomyia fasciata* and *Culex pipiens*, some of which were of sufficient interest to record.

We found that the female *Stegomyia* does not always lay her eggs at one time. More often she deposits them in groups at intervals of several days. The maximum number laid by any one insect observed by us was 101. The female *Stegomyia* sometimes dies, apparently from exhaustion, after laying her eggs, but we noted several instances in which this was not the case. The insect which laid 101 eggs was alive and vigorous until killed by us five days later.

The manner in which the female *Stegomyia* lays her eggs is of some interest. She bends her abdomen ventrally, and as the genital orifice comes in contact with the sides of the vessel or with the water or other object the egg is deposited. The insect moves along and repeats the performance.

The eggs are sometimes laid on the water, sometimes on the side of the vessel above the water line, and sometimes on a leaf floating on the water.

In accordance with the few observations which we made on this particular point, *Stegomyia fasciata* females that are fed solely on banana or sugar do not lay eggs. They seem to require a feeding of blood for ovipositing. Unconjugated females also do not lay eggs.

The longest life that we observed was in a female *Stegomyia*, which we kept for sixty-four days, and then killed for sectioning.

We found, as has been often noted by other observers, that the greatest activity of the *Stegomyia fasciata* is during the daytime, but we have observed them flying at night. We have also observed them feeding on us at night by artificial light. We have noticed on several occasions that they are especially voracious early in the morn-

ing, about sunrise. On several occasions a number of noninfected insects were let loose in the laboratory and we observed that upon rising at sunrise they attacked us viciously.

It may be noted that this fact apparently explains the danger to persons sleeping in an infected house and the comparative freedom from danger in daylight communication with an infected town, especially if the person remains in the open air and sunlight and avoids houses, and confines his visits to the streets and parts of the town free from the disease.

A number of experiments were made with the female *Culex pun-gens*, but they could not, under any circumstances, be induced to feed upon blood while in confinement. It was found that they preferred death.

MOSQUITOES MAY BITE CADAVERS.

The female *Stegomyia fasciata* will bite a cadaver, and, if on a dependent portion, can draw blood. We have two observations on this point.

Narciso Nadal (case XX). A number of *Stegomyia* were applied twelve hours after death, only one of which apparently obtained blood.

Trinidad Martinez (case XXII). A number of female *Stegomyia fasciata* were applied one-half hour after death, and three insects succeeded in feeding with blood.

As it has been shown by the work of the French commission that the blood of yellow fever is not infective after the third day, the danger of conveying the infection by means of mosquitoes feeding upon cadavers must be exceedingly remote.

LONGEVITY.

Several experiments were undertaken to determine the fact whether the male *Stegomyia fasciata*, as has been stated, has a brief life history. We have one experiment showing that the male mosquito may live and thrive over a month.

Observation.—A number of male mosquitoes were placed in a cage October 10 and subsequently fed on sirup. They were all alive and in good condition on November 15, when they were killed and used for experimental purposes, having lived thirty-six days.

OVIPOSITING.

Sometimes the female *Stegomyia fasciata* will lay a considerable number of eggs at one time and then die.

Observation.—(Mosquito XLIII. Francis, Re. No. 4.) This female *Stegomyia fasciata* was taken from the breeding jar on October 3, fed on normal blood October 4, 6, 7, 8, and 10, then placed in a jar with water to tempt ovipositing, and banana feeding begun. On October 19 four males were added to the jar. On October 23 the female was given another blood feed. On the 26th

she laid 54 eggs and was found exhausted and dying on the surface of the water.

More often the female *Stegomyia* lays groups of eggs at intervals of several days, and sometimes lives after the last laying.

Observations.—(Mosquito XLIII-38. Francis, Rc. No. 1.) This female *Stegomyia* was taken from the breeding jar October 3; fed on normal blood on October 4, 6, 7, 8, and 10; then placed in a jar to tempt ovipositing and given banana; laid eggs on October 10 and 11; given another blood feed October 16; found apparently dying on the surface of the water on October 18.

(Mosquito XLIII-68. Francis, Rc. No. 3.) This female *Stegomyia* was taken from the breeding jar on October 3 and fed on normal blood October 4, 6, 7, 8, and 10. It was then placed in a jar to tempt ovipositing and given banana. On October 11 she laid a considerable number of eggs. On October 19 again given blood feed and three males placed in the jar. October 25 she laid 29 eggs. On October 26 laid 12 more eggs. On the 30th the insect was removed in a dying condition.

(Mosquito XLIII-67. Francis, Rc. No. 5.) This female *Stegomyia* was taken from the breeding jar October 3. Fed on normal blood October 4, 6, 7, 8, and 10. Then placed in a separate jar with water to tempt ovipositing and given banana. On October 13 she laid some eggs. On the 19th given a blood feed and three males added. She laid 11 more eggs on October 23, 16 on the 25th, and 37 on the 28th, when she was found dying on the surface of the water.

(Mosquito XLIII-69. Francis, Rc.) This female *Stegomyia* was taken from the breeding jar when less than forty-eight hours old and fed upon normal blood October 4, 6, 7, 8, and 10, and subsequently at intervals of one or two days up to October 23, when she was placed in a cage by herself with a beaker of water to tempt ovipositing. At the same time given banana to feed upon. October 25 two males were added to the cage. October 25 she laid 51 eggs; November 7, 24 eggs; November 8, laid 26 eggs; total, 101 eggs.

She was given another feed of blood November 10.

Was killed November 13 while apparently vigorous.

Female *Stegomyia fasciata* that have fed on the blood of yellow-fever patients on the second, fourth, and sixth days of the disease may subsequently lay eggs that hatch in a normal manner, and the larvae develop into pupæ and imagoes.

Observations.—(Mosquito XLVII-36. Marcial Lujan, Rx. a.) This insect was separated from the breeding jar October 8 and fed on Marcial Lujan, a typical case of yellow fever on the sixth day of his illness. She was subsequently fed on normal blood October 11, 13, 16, 17, and 19. On October 22 a beaker of water was placed in the cage in order to tempt ovipositing, and banana feeding begun. She laid 15 eggs on October 25 and 15 more on October 26. Both sets hatched.

(Mosquito XLVII-37. Marcial Lujan, Rx. b.) This female *Stegomyia* taken from the breeding jar October 8. Fed on blood of Marcial Lujan on the sixth day of his illness, October 9, and subsequently on normal blood October 11, 13, 16, 17, and 19. On October 22 given a beaker of water to tempt ovipositing and banana feeding begun. She laid 31 eggs on October 26, 9 on the 27th, and 12 on the 30th. The eggs laid on the 26th and 27th hatched on the 29th.

(Mosquito XLII-122. Marcos Cruz, Rn. a.) This insect was separated from the breeding jar October 14 and allowed to feed on Marcos Cruz, one of our experimental cases of yellow fever October 15, that is, on the second day of his

Illness. She was subsequently fed on sirup. On November 1, placed in a cage with a beaker of water and two males. She laid 12 eggs on November 4, which subsequently hatched.

(Mosquito LVIII-32. Sesoleda Martinez, Rx. b.) This female *Stegomyia* was separated from the breeding jar October 19. Fed upon the blood of Sesoleda Martinez, a fatal case of yellow fever October 20, the fourth day of his illness. Subsequently this insect was given banana. October 28 a normal blood feed. On November 5 a beaker of water was placed in the cage to tempt ovipositing. Four days later, November 9, she laid 26 eggs, which subsequently hatched.

The statement has been made that the female *Stegomyia fasciata*, and mosquitoes generally, require a feeding on blood in order to lay eggs. In three experiments tried by us we are able to confirm this statement so far as the *Stegomyia fasciata* is concerned. The insects were fed on sirup and banana, but could not be tempted to lay eggs.

Observations.—Banana feeding. A large number of male and female *Stegomyia fasciata* that had been fed on banana for fourteen days were given a beaker of water to tempt ovipositing. They were left nine days. No eggs laid. They were then killed for section.

Sirup feeding. A large number of male and female *Stegomyia* that had been fed on sirup for fourteen days were given a beaker of water to tempt ovipositing. They were observed twenty-one days later. No eggs were laid.

Banana and sirup feeding. A large number of male and female *Stegomyia* were given alternate feedings of banana and sirup for thirty-two days, at which time a beaker of water was placed in their cage to tempt ovipositing. They were observed nine days later. No eggs were laid.

Unconjugated females do not lay eggs.

Observations.—Stegomyia pupæ were isolated and placed in separate small bottles so that the imagoes could not be kept in strict quarantine. Six of these unconjugated females were given a feeding of blood twenty-four hours after birth, and were subsequently fed on banana. They were kept in a cage with a beaker of water to tempt ovipositing. Five days subsequently they were given a second feeding on blood. Twenty-five days later they were killed, not having laid eggs.

SIZE OF SCREENING.

It is of considerable practical importance in quarantine and public health work to know the size of screening that will keep out the *Stegomyia fasciata*, and as no accurate observations upon this subject had been made, with which we were familiar, we conducted a few experiments to determine this point.

Screens with a varying number of meshes to the inch were placed over breeding jars, and banana, sirup, and other food placed on the other side so as to tempt the hungry insects to pass through. These experiments were arranged by placing the fruit and food in a jar which was inverted over the breeding jar. A piece of gauze or netting was inserted between the two jars so that the *Stegomyia* would have to pass through its meshes in order to appear in the upper jar.

We found that both male and female *Stegomyia* may pass a wire

gauze containing 16 strands or 15 meshes to the inch, but could not pass 20 strands or 19 meshes to the inch.

It is therefore evident that the large-meshed mosquito bars ordi-

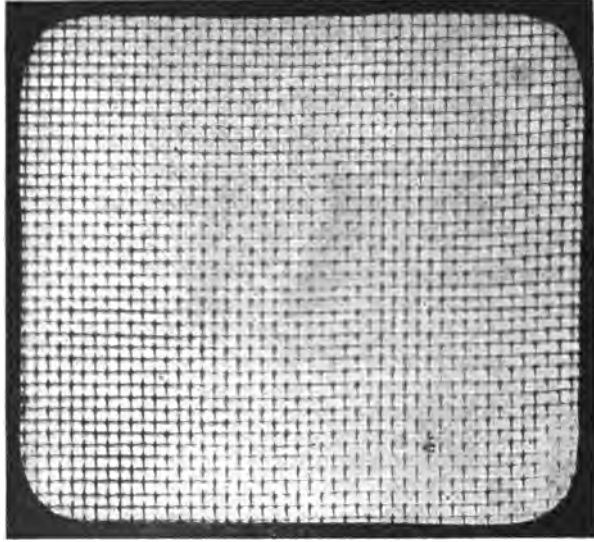


FIG. 4.—Showing screen containing 16 strands or 15 meshes to the inch. Allows male and female *stegomyia fasciata* to pass.

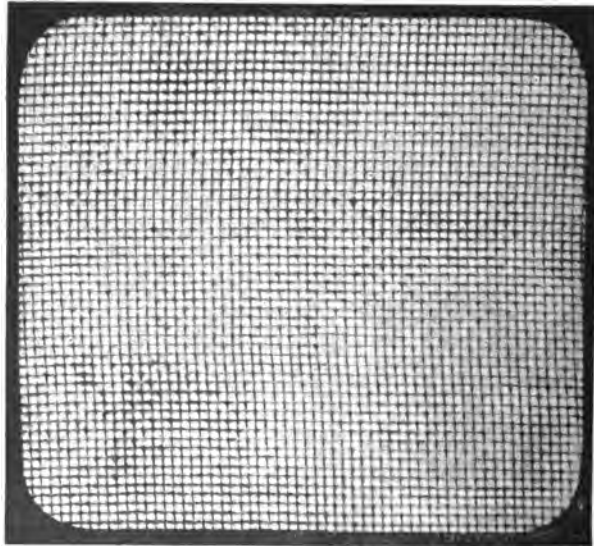


FIG. 5.—Showing screen containing 20 strands or 19 meshes to the inch, through which *stegomyia fasciata* can not pass.

narly used in this latitude would not offer proper protection, and that window screening must also be of a finer wire than is sometimes employed.

DISINFECTION EXPERIMENTS.

A few tests were made to determine the relative efficiency of sulphur dioxide, tobacco smoke, and pyrethrum as insecticides with particular reference to the *Stegomyia fasciata*.

A small room and hallway containing 1,200 cubic feet of air space were used in these experiments. The room contained a large window and one door, which were made reasonably tight to prevent the escape of the fumes, and the mosquitoes were exposed in cages in various parts of the room.

Experiment No. 1—Tobacco.—One pound of tobacco per 1,000 cubic feet; exposure, one hour; result, some mosquitoes survived.

Six hundred and twenty-five grams of tobacco, which is about the proportion of 1 pound per 1,000 cubic feet, were burned in a pan in the center of the room. The cages containing the mosquitoes were placed on the floor, near the ceiling, and on a chair.

The room was opened one hour after the tobacco was lighted, which was done by means of alcohol. The mosquito cages were immediately removed and placed in a current of fresh air in order to give the mosquitoes a favorable opportunity to revive.

All the mosquitoes in the cage which was near the ceiling were dead. Of those in the cage on the chair, one female was flying actively about; the other females and another male were all dead. Those in the cage that stood on the floor were stupefied, but none was killed, most of them flying actively about.

The tobacco was completely consumed in this process, and the fumes upon opening the door were very strong. The unpleasant odor was very persistent and disagreeable.

Experiment No. 2—Tobacco.—Two pounds per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

The mosquito cages were immediately removed after two hours had elapsed, at which time none of the insects showed apparent signs of life; but after remaining in the fresh air for three hours a few of them moved their wings and tarsi. None, however, revived.

Experiment No. 3—Pyrethrum.—Two pounds per 1,000 cubic feet; exposure, 2 hours; result, all mosquitoes killed.

The pyrethrum was burned in a brazier placed upon some sand on the floor.

Three cages containing many mosquitoes were distributed, one on the floor, one near the ceiling, and one in an open box on the table. The cages had a piece of crumpled gauze upon the bottom and a folded handkerchief hanging in the cage, in order to give the insects retreats in which to hide from the effects of the fumes and to test the penetrating action of the gas.

All of the mosquitoes were killed.

Experiment No. 4—Pyrethrum.—Two pounds per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

Mosquito cages were placed in several parts of the room. At the end of the experiment some of the insects showed signs of life, but none revived.

Experiment No. 5—Pyrethrum.—One pound per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

The pyrethrum was burned in an open brazier upon the floor in the same room used for the preceding experiments. The mosquitoes were freely exposed to the effects of the fumes in appropriate cages, which were placed upon the floor, near the ceiling, and one inside a box laid upon a table.

At the end of the experiment the cages were immediately taken to the fresh air and many of the *Stegomyia* showed signs of life, but none revived.

Experiment No. 6—Sulphur.—Three and one-fourth pounds per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

In this experiment four large rooms and the hallway of our laboratory building were fumigated to destroy some mosquitoes that had escaped. The rooms communicated with each other and with the hallway through large openings. No attempt was made to seal the doors and windows or to paste cracks.

Three pots of sulphur were distributed at points of vantage, each pot containing 20 pounds, the total space to be fumigated being 12,280 cubic feet.

Two hours after the sulphur was lighted the house was opened and it was found that only about two-thirds of the sulphur had burned; that is, about 3½ pounds per 1,000 cubic feet. In this experiment the pots containing the sulphur were not placed in water, the object being to obtain a dry gas and thereby minimize the destructive action of the fumes upon the fabrics and pigments.

Four cages containing mosquitoes were placed in different parts of these rooms and all were killed.

As a result of these disinfection experiments we conclude that: While we found tobacco smoke efficacious in destroying the insects, we also found that the method is exceedingly objectionable on account of the persistent and disagreeable odor that it leaves, as well as on account of the yellow stains which remain. Tobacco smoke in concentrated form stains fabrics, paint work, and other surfaces, but the stains may be removed by washing; still, this forbids its use in parlors and the rooms of fine houses.

We found that the burning of 1 pound of tobacco per 1,000 cubic feet, with an exposure of one hour, was only sufficient to stupefy the insects. All *Stegomyia fasciata* were killed by an exposure of two



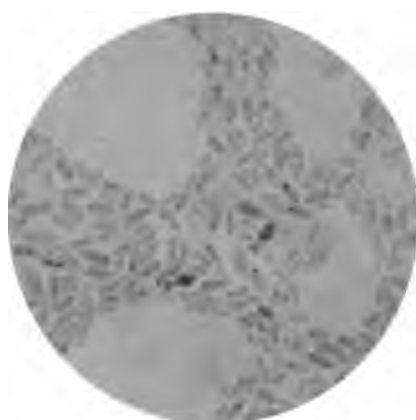
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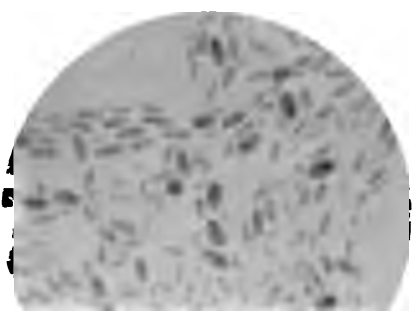
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5



6

WILD YEAST IN PURE CULTURE ISOLATED FROM BANANA AT VERA CRUZ, MEXICO,
IN THE SUMMER OF 1903. STAINED WITH HEMATOXYLIN AND EOSIN.
ALL THE SPECIMENS SHOW DEEPLY STAINED GRANULES.

hours to the fumes of tobacco burned in a proportion of 2 pounds per 1,000 cubic feet.

We found 1 pound of pyrethrum per 1,000 cubic feet, with an exposure of two hours, sufficient to kill *Stegomyia fasciata*, and, although many of them still showed signs of life after this exposure, none revived. Two pounds per 1,000 cubic feet, with an exposure of two hours, was sufficient to kill them outright.

We made only one experiment with sulphur dioxid in order to kill some *Stegomyia fasciata*, which had escaped in the laboratory. We selected sulphur on account of our confidence in the insecticidal value of this substance. In this experiment we used about 3 per cent of the gas, generated by burning in open pots, with an exposure of two hours. The previous work of one of us^a showed that 1 per cent, with an exposure of one hour, is quite sufficient in a small inclosure, but we used the excess on account of the peculiar construction of the house.

When burning sulphur for its insecticidal effects care should be taken to keep the gas as dry as possible, while the contrary is necessary in order to obtain its germicidal action.

The small percentages of sulphur dioxid kept dry are not sufficient during short exposures to bleach pigments or injure fabrics; and this, in our opinion, is the best of the poisonous gases to insure the destruction of such vermin in houses. Formaldehyde gas is utterly untrustworthy in this connection. It is not an insecticide.

We made no experiments with hydrocyanic-acid gas. While recognizing its great insecticidal power, we considered it entirely too poisonous a substance to use in the household or other inhabited places. In our opinion the use of this gas should be limited to greenhouses, railroad cars, granaries, and other isolated and uninhabited places.

SUMMARY AND CONCLUSIONS.

The cause of yellow fever is not known.

The *Myxococcidium stegomyiae* is not an animal parasite. Yeast cells sometimes simulate the coccidia in form and staining reaction.

The infection of yellow fever is in the blood serum early in the disease. No abnormal elements that bear a causal relation to the disease can be detected in the serum or in the corpuscles with the best lenses at our command.

^aDisinfection against mosquitoes with formaldehyde and sulphur dioxid, M. J. Rosenau. Bull. No. 6, Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv., Wash., Sept. 1901.

YELLOW FEVER INSTITUTE, BULLETIN No. 14.

Treasury Department, U. S. Public Health and Marine-Hospital Service.

WALTER WYMAN, *Surgeon-General.*

REPORT

OF

WORKING PARTY No. 2,

YELLOW FEVER INSTITUTE.

EXPERIMENTAL STUDIES IN YELLOW FEVER AND MALARIA
AT VERA CRUZ, MEXICO.

BY

M. J. ROSENAU, PASSED ASSISTANT SURGEON.
HERMAN B. PARKER, PASSED ASSISTANT SURGEON.
EDWARD FRANCIS, ASSISTANT SURGEON.
GEORGE E. BEYER, ACTING ASSISTANT SURGEON.

MAY, 1904.

WASHINGTON:
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1905.

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PREFACE AND ACKNOWLEDGMENTS.

Working Party No. 2, Yellow Fever Institute, consisting of Passed Asst. Surg. Herman B. Parker, Asst. Surg. Edward Francis and Acting Asst. Surg. George E. Beyer, was detailed by the Surgeon-General U. S. Public Health and Marine-Hospital Service, with the approval of the Secretary of the Treasury, to Vera Cruz, Mexico, April 27, 1903, for the purpose of making further studies upon the cause and methods of transmission of yellow fever.

Doctor Parker returned to Washington upon official business June 7, 1903, and on September 13, 1903, returned to Vera Cruz with Passed Asst. Surg. M. J. Rosenau, Director of the Hygienic Laboratory, who had in the meantime been appointed chairman of the commission, with instructions to repeat that part of the work of Working Party No. 1 relating to the *Myxococcidium stegomyia*.

Professor Beyer left for New Orleans on October 4 to resume his duties at the Tulane University of Louisiana.

The remaining three members of the working party continued work at Vera Cruz until November 28, 1903, when, on account of the subsidence of the yellow fever epidemic and scarcity of material, they returned to Washington.

The commission made a brief report to the Surgeon-General, signed by all of its members and published in the Public Health Reports for January 15, 1904, as follows:

Findings of Working Party No. 1, Yellow Fever Institute, not all corroborated by Working Party No. 2.

WASHINGTON, December 18, 1903.

SURGEON-GENERAL.

SIR: We have the honor to report that, as a result of our studies at Vera Cruz, Mexico, this summer, we have not been able to corroborate all the findings of Working Party No. 1, Yellow Fever Institute, Public Health and Marine-Hospital Service, having found phases of the organism described by them as *Myxococcidium stegomyia* in normal mosquitoes.

Respectfully,

M. J. ROSENAU,
Chairman Working Party No. 2.

H. B. PARKER,
EDWARD FRANCIS,
GEO. E. BEYER.

The commission was now, January 18, 1904, dissolved, and its members permitted to publish individually any further matter bearing on the summer's work.

This bulletin, therefore, has been prepared by two members of the commission, Doctors Rosenau and Francis, who have continued certain phases of the work, but who here wish to make full acknowledg-

YELLOW FEVER INSTITUTE, BULLETIN No. 15.

Treasury Department, U. S. Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

REPORT
OF
WORKING PARTY NO. 3,
YELLOW FEVER INSTITUTE.

ATTEMPTS TO GROW THE YELLOW FEVER PARASITE.

**THE HEREDITARY TRANSMISSION OF THE YELLOW FEVER
PARASITE IN THE MOSQUITO.**

BY

M. J. ROSENAU

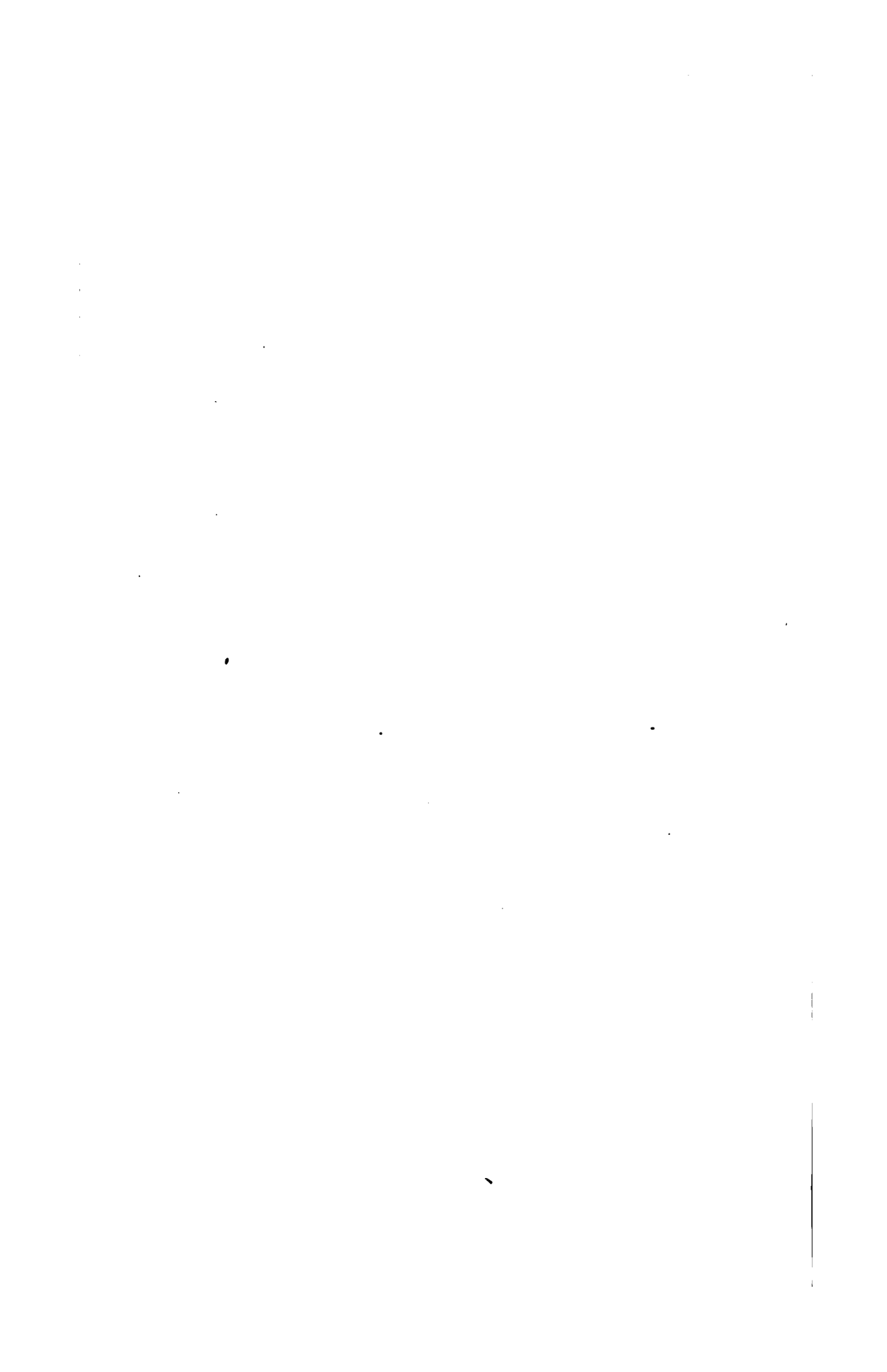
AND

JOSEPH GOLDBERGER.

JANUARY, 1906.

WASHINGTON:
GOVERNMENT PRINTING OFFICE.

1906.



YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 15.

Section B.—ETIOLOGY.

P. A. Surg. M. J. ROSENAU, Chairman of Section.

ATTEMPTS TO GROW THE YELLOW FEVER PARASITE.

THE HEREDITARY TRANSMISSION OF THE YELLOW FEVER PARASITE IN THE MOSQUITO.

By M. J. ROSENAU, *Passed Assistant Surgeon,*
and

JOSEPH GOLDBERGER, *Passed Assistant Surgeon,*
U. S. Public Health and Marine-Hospital Service.

ATTEMPTS TO GROW THE YELLOW FEVER PARASITE.

In view of the fact that the infective principle causing yellow fever may pass through the close-grained pores of a Pasteur-Chamberland B filter, it seemed to us hopeless, with the limitations of the present microscope, to expect to see the causative agent of this disease by direct examination of the blood.

Novy's work with trypanosomes, both his success in their artificial cultivation and his filtration experiments indicating the possibility of an "ultramicroscopic" phase in their developmental cycle, suggested to us the possibility of cultivating by similar methods the yellow fever parasite and thus perhaps developing a stage in its life cycle which might readily be visible. We attempted, therefore, to grow the parasite of yellow fever in the "water of condensation" of blood-agar tubes.

The culture tubes were prepared in several different ways; both human blood (nonimmune) and rabbit's blood were used. Some tubes were prepared with the whole, and some with the defibrinated blood. When

the whole blood was used it was quickly added while fresh to melted agar, at 42° C., in the proportion of about 2 parts of blood to 1 of agar. After mixing, the tubes were slanted and allowed to set. The defibrinated blood was prepared by whipping in the usual way, and then it was added to the melted agar in about the same proportions as above stated. After standing a short while the blood-agar slants, thus prepared, developed from several drops to about 1 cc. of "water of condensation."

A drop or two of blood from typical cases of yellow fever taken from the arm vein during the early stages of the disease was planted into this "water of condensation."

Other cultures were prepared with much larger quantities of the yellow fever blood, using the yellow fever blood itself as a part of the culture medium. To tubes containing about 2 cc. of melted agar, about 4 cc. of fresh yellow fever blood was added as quickly as possible after its withdrawal from the vein. Other tubes were similarly prepared with the defibrinated yellow fever blood.

Some of the cultures were kept in the incubator at 37° C., and others at room temperature. Of the latter, some were kept in the dark and others exposed to the light in order to simulate the conditions as they appear to occur in the mosquito.

The water of condensation was examined from time to time both in hanging drop and in stained smears. It was found to contain large numbers of bodies of various sizes and shapes, some of them exhibiting curious and exaggerated Brownian motion. All of the particles were interpreted as degeneration products, mostly from the cellular elements of the blood.

HEREDITARY TRANSMISSION OF THE YELLOW FEVER PARASITE IN THE MOSQUITO.

The question of the hereditary transmission of the yellow fever parasite from the *Stegomyia fasciata* to its progeny is of interest both biologically and practically.

Reasoning by analogy such transmission can not be regarded as impossible, as it is known to occur in some, probably closely allied diseases, namely through the tick in Texas fever^a and canine piroplasmosis^b. Schaudinn^c has satisfied himself that hereditary transmission of the tertian malarial parasite (*Plasmodium vivax*) occurs in *Anopheles*, and recently Dutton and Todd^d have shown that the spirochaete of the tick fever of the Congo is passed from tick to tick through the egg.

To the sanitarian the question is of interest in its bearing on the problem of the recrudescence of yellow fever.

The recrudescence of epidemics of yellow fever has heretofore been explained in one of two ways: (1) Either a *Stegomyia fasciata* that had become directly infected by feeding on a case of the disease had survived (as they are experimentally known to be able to do), or (2) the infection had in the interval between the epidemics been continued by unrecognized cases and on the recurrence of favorable conditions the disease would reassume epidemic proportions.

From time to time a third explanation has been advanced, namely, the transmission of the infection from the mother mosquito through the eggs to its progeny^e which, under favorable circumstances, were

^a Smith and Kilborne, 1893, U. S. Department of Agriculture, Bureau of Animal Industry, Bulletin No. 1.

^b Lounsbury, C. P., Transmission of Malignant Jaundice of the Dog by a Species of Tick. Reprint Cape of Good Hope Agricultural Journal, November 21, 1901.

^c Schaudinn, Fritz, Generations und Wirtswechsel bei Trypanosoma und Spirochaete. Arbeiten aus dem Kaiserlichen Gesundheitsamte, Berlin, Band XX, Heft 3, 1904, p. 428.

^d Dutton and Todd, Liverpool School of Tropical Medicine, Memoir xvii, 1905.

^e Finlay (Medical Record, N. Y., May 27, 1899, p. 738), inspired by the discovery of Smith and Kilborne of the hereditary transmission of the parasite of Texas fever in the tick, was the first to suggest the hereditary transmission of the yellow fever parasite in the mosquito. In 1901 Reed, Carroll, and Agramonte (American Medicine, Phila., July 6, 1901, p. 19) reported the negative results of an inoculation experiment with 14 mosquitoes hatched from the ova of a *Stegomyia fasciata* that had already shown itself capable of conveying the disease, and Guiteras (American Medicine, Phila., Nov. 23, 1901, p. 810) reports two experiments. In both the mother

capable without themselves directly having had access to a case of yellow fever, of giving the disease to a susceptible individual. This explanation has now received the support of an experimental case of yellow fever induced by the sting of a *Stegomyia fasciata* apparently hereditarily infected. This case is reported by Marchoux and Simond in a paper on "The hereditary transmission of the yellow fever virus in the *Stegomyia fasciata*," a translation of which we give in appendix, p. 114.

Against this one positive case we submit the negative results of inoculations attempted in 13 nonimmunes.

In an endeavor to account to ourselves for the divergence of our results from that of the French workers we have considered several factors in the problem, failure to comply with any of which might readily be productive of negative results. We believe, however, that our work, so far as we can judge from the details in their paper, closely parallels the work of Marchoux and Simond. Naturally the first factor which arises for consideration is whether the mothers of the *Stegomyia fasciata* used by us for the inoculation of our nonimmunes were infected. Marchoux and Simond state that the mother of the insect whose sting produced the positive case of fever had been made to feed on *several* (number not stated)^a of their

mosquitoes were experimentally proved to be infected. In the first the progeny of one mother were tried without results upon three nonimmunes; in the other a large brood from several mosquitoes was kept in a breeding jar and was fed upon nonimmunes with impunity.

^aDuring the progress of this bulletin through the press the second report of the French Commission to Rio de Janeiro (Marchoux and Simond, *Annales de l'Institut Pasteur*, Paris, XX, 2, Jan. 25, 1906, p. 16) came to our hands, giving full details of the positive experimental case of yellow fever produced by the sting of a *Stegomyia fasciata* apparently hereditarily infected, as follows:

"Experiment.—A female *Stegomyia fasciata* born in the laboratory and arriving at the adult stage January 19 (*probably means January 9*), 1905, was paired from the 9th to the 11th. It stung a yellow-fever patient presenting a severe attack in the second day of the disease, on the 11th of January, and laid the first batch of eggs January 17. On the 25th of January it stung another patient in the second day of the disease, who presented an attack of moderate severity, and laid the second batch of eggs January 28. This latter batch hatched out from the 3rd to the 4th of February, and the larvæ cared for in the laboratory produced perfect insects February 16.

"Two females from this batch were isolated in tubes and fed with sirup up to March 2. At this date—that is to say, 14 days after completing their metamorphosis, these mosquitoes were made to sting subject A. This subject, a Portuguese, had arrived in Brazil only a few days before and had never had yellow fever. He showed no reaction to this inoculation. After an interval of eight days, March 10, the same subject was stung a second time by one of the two mosquitoes, the other having accidentally died. Four days later, March 14, he presented symptoms of yellow fever."

It will be noted, therefore, that the eggs giving rise to the progeny that apparently caused an attack of yellow fever were laid by the mother mosquito 17 days after the first and 3 days after the second feed of yellow-fever blood. (Compare our mosquitoes Nos. 3 and 4, Group II, of Set 1, p. 107.)

cases of yellow fever in order to determine a heavy infection. In our work mother mosquito of Set 1 had three feedings of yellow fever blood from two severe cases.

Mother mosquito of Set 2 and that of Set 3 each had one feed of yellow fever blood early in the disease.

That the interval between the infecting feed and oviposition must enter as an important element in the transmission of the infection through the eggs to the progeny—if such transmission ever takes place in yellow fever—must be evident. Marchoux and Simond do not report clearly on this point;^a they state simply that their mosquito was 20 days old at the time of oviposition and that some time prior to the laying it had been made to sting several cases of yellow fever.

In our experiments the intervals were as follows:

SET 1.

Group I, mosquitoes Nos. 1 and 2.—The eggs producing these mosquitoes were laid 13½ days from the first, 11½ days from the second, and about 2½ days after the third feed of yellow fever blood.

Group II, mosquitoes Nos. 3 and 4.—The eggs giving rise to this group were laid 16 days from the first, 14 days from the second, and about 5 days from the third feed of yellow fever blood. (Compare footnote (a), page 106.)

SET 2.

Group I, mosquito No. 5.—The eggs giving rise to this group were laid 15 days after one feed of yellow fever blood.

SET 3.

Group I, mosquito No. 6.—The eggs giving rise to this group were laid 14 days after one feed of yellow fever blood.

Groups II, III, and IV, mosquitoes Nos. 7, 8, 9, 10, 11, 12, 13, and 14.—The eggs giving rise to these groups were laid 15 days after one feed of yellow fever blood.

Another important factor in the problem, and one to which Marchoux and Simond call attention, is the time needed by the hereditarily infected mosquito to become infective. In their case this was twenty-two days. In our work the inoculations were carried up to and including at least the forty-ninth day, as shown in Table 1.

^aSee note a on page 106.

TABLE 1.—Summary of inoculations of nonimmunes by hereditarily infected (?) mosquitoes—subjects kept under observation at least seven days after each inoculation.

[The mosquitoes are designated by numbers from 1 to 14; nonimmunes by capital letters.]

Mosquito.	Stung nonim-mune	Age of mosquito at time of stinging.	Remarks.	Mosquito.	Stung nonim-mune	Age of mosquito at time of stinging.	Remarks.
		<i>Days.</i>				<i>Days.</i>	
No. 10	B	2	No reaction.	Nos. 6 and 10 ...	G	26	No reaction.
Nos. 7, 8, and 9 ..	B	3	Do.	No. 14	a L	26	Do.
No. 2	A	6	Do.	Nos. 5 and 9	F	27	Do.
No. 1	B	9	Do.	No. 6	H	28	Do.
No. 2	C	10	Do.	Nos. 3 and 4	G	29	Do.
No. 2	A	12	Do.	Nos. 12, 13, and 14	b M	30	Do.
Nos. 1 and 2	C	13	Do.	No. 6	J	31	Do.
Nos. 3 and 4	B	13	Do.	Nos. 1, 11, and 12.	B	32	Do.
Nos. 1 and 2	B	20	Do.	No. 8	J	33	Do.
No. 3	E	21	Do.	No. 6	M	34	Do.
Nos. 11 and 12 ..	H	22	Do.	Nos. 12, 13, and 14	G	34	Do.
No. 4	E	23	Do.	No. 1	H	35	Do.
Nos. 13 and 14 ..	J	23	Do.	Nos. 12 and 13 ..	J	36	Do.
Nos. 1 and 2	D	24	Do.	No. 3	b L	37	Do.
No. 6	F	24	Do.	No. 1	K	39	Do.
Nos. 5 and 9	F	25	Do.	Nos. 13 and 14 ..	N	39	Do.
Nos. 11 and 12 ..	J	25	Do.	No. 12	N	40	Do.
No. 13	G	25	Do.	No. 3	G	45	Do.
No. 3	F	26	Do.	No. 3	N	49	Do.

a Subject passed from observation after 6 days.

b Subject passed from observation after 5 days.

A factor in the problem which is of prime importance and which must always be reckoned with in estimating the value of negative results is the susceptibility to the disease of the subject used for the inoculations. We were careful to select only those who we were satisfied never had had the disease.

Another factor which must be considered is temperature. No mention is made in the paper of Marchoux and Simond at what temperature their mosquitoes were kept. Our mosquitoes were kept under artificial conditions at a temperature of between 80° and 90° F. (See p. 109.)

Many other factors which we shall not discuss undoubtedly enter into and affect this problem.

DETAILS OF EXPERIMENTS.

In our study we used three sets of *Stegomyia fasciata*, comprising fourteen insects, the progeny of three mothers that had fed on yellow fever. The history of these mosquitoes is as follows:

Set 1, Groups I and II, mosquitoes Nos. 1, 2, 3, and 4.

Mother mosquito.—The mother mosquito of this set was one of a number raised from the larval stage in our laboratory, and, without any prior feeding, was made to sting, on October 3, at 5.20 p. m., a patient (Melancon) with a severe case of yellow fever, 14½ hours after the initial chill; about 42 hours later this mosquito was again made

to sting the same patient, now about 56 hours after the onset. On October 14, at 3.55 p. m., this insect was made to sting a second yellow fever patient (Kippers), suffering from a severe attack of the disease, about 48 hours after the onset of the first symptoms.^a In all, then, this mosquito had three feedings of yellow fever blood from two severe cases in the early stages of the disease. This, as well as all our mosquitoes, was kept in a room in which the temperature was artificially kept between 80° F. and 90° F. Four or five times throughout the course of these experiments the temperature in this room fell to 70° for six or eight hours at a time.

Group I.—On October 17, at 8.30 a. m. (13½ days from the first, 11½ days from the second, and about 2½ days from the third feed of yellow fever blood), this mosquito deposited eggs from which there were hatched between November 4 (4 p. m.) and November 5 (8.30 a. m.) two^b adult female *Stegomyia fasciata*, which comprise our Group I of Set 1, and were numbered 1 and 2.

Group II.—On October 19, at 4.30 p. m. (16 days from the first, 14 days from the second, and about 5 days from the third feed of yellow fever blood), this same mother insect laid a second batch of eggs from which were hatched between November 7 (8 a. m.) and November 8 (8.30 a. m.) two adult female *Stegomyia fasciata*, which comprise our Group II of Set 1, and were given the numbers 3 and 4.

Set 2, Group I, mosquito No. 5.

Mother mosquito.—The mother mosquito of this set was one of a number raised from larvæ and for some time fed on immune blood.

On October 4, at 9 a. m., this insect was made to sting a severe case (Melancon) of yellow fever 30 hours after the initial chill.^c

Group I.—October 19, at 4.30 p. m. (15 days after the feed of yellow fever blood), this insect laid a batch of eggs from which there was hatched between November 7 (8.30 a. m.) and November 9 (8.30 a. m.) one adult *Stegomyia fasciata*, which was given the number 5 and was the only one comprised in this set.

Set 3, Groups I, II, III, and IV, mosquitoes Nos. 7, 8, 9, 10, 11, 12, 13, and 14.

Mother mosquito.—The mother mosquito of this set was one of a number of *Stegomyia fasciata* raised from larvæ in our laboratory

^a On Oct. 8, 10, and 12, it was permitted to fill itself by stinging an immune. After Oct. 16, fed with sirup.

^b We mention only the mosquitoes that survived and were used for inoculation; others, including males, are ignored in this report.

^c On Oct. 6, 8, 10, 12, and 15, fed by stinging an immune. After Oct. 16, fed with sirup.

and, without any prior feeding, was made to sting on October 4, at 9 a. m., a severe case of yellow fever (Melancon) 30 hours after the initial chill.^a

Group I.—October 18, at 4.20 p. m. (14 days after the feed of yellow fever blood), this insect deposited some eggs, from which there was hatched November 12, at 9 a. m., an adult female *Stegomyia fasciata*, which formed Group I of this set and was given the number 6.

Group II.—October 19, at 4.30 p. m. (15 days after the feed of yellow fever blood), this mother mosquito laid another batch of eggs, from which there were hatched between November 7 (8.30 a. m.) and November 9 (8.30 a. m.) three female *Stegomyia fasciata*, numbered 7, 8, and 9, which form Group II of this set.

Group III.—November 12, at 9 a. m., there was hatched an additional adult female *Stegomyia fasciata*, which was numbered 10 and forms Group III of this set.

Group IV.—Between November 13 (8.30 a. m.) and November 18 (8.30 a. m.) there were hatched four additional females, numbered 11, 12, 13, and 14, which comprise Group IV of this set.

At stated intervals these fourteen *Stegomyia fasciata*, the progeny of mothers (Sets 1, 2, and 3) that had fed on cases of yellow fever as above indicated, were made to sting nonimmune subjects, and during the intervals fed upon sirup.

Mosquitoes Nos. 1 and 2 (Set 1, Group I) were applied to and stung seven nonimmunes (A, B, C, D, G, H, K) at various intervals between the sixth and thirty-ninth day after completing their metamorphoses, as shown in Table 2.

TABLE 2.—*Inoculation with mosquitoes Nos. 1 and 2.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
No. 2	A	6-7	Nos. 1 and 2	B	20-21
No. 1	B	9-10	Nos. 1 and 2	D	24-25
No. 2	C	10-11	No. 1	G	32-33
No. 2	A	12-13	No. 1	H	35-36
Nos. 1 and 2	C	13-14	No. 1	K	39-40

Of these inoculations, four were made after the twenty-second day (the mosquito incubation period in the successful case reported by Marchoux and Simond), namely, at age periods of 24, 32, 35, and 39 days.

^a On Oct. 6, 8, 10, 12, and 14, fed by stinging immune. After Oct. 15, fed with sirup.

Mosquitoes Nos. 3 and 4 (Set 1, Group II) were made to sting eight nonimmune subjects (B, E, F, G, J, L, M, and N) ten times at intervals between the thirteenth and forty-ninth day after emergence as adult insects, as shown in Table 3.

TABLE 3.—*Inoculation with mosquitoes Nos. 3 and 4.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
Nos. 3 and 4.....	B	13-14	No. 3.....	J	33-34
No. 3.....	E	21-22	No. 3.....	^a L	37-38
No. 4.....	E	23-24	No. 3.....	M	42-43
No. 3.....	F	26-27	No. 3.....	G	45-46
Nos. 3 and 4.....	G	29-30	No. 3.....	N	49-50

^a Subject passed from observation at the end of 5 days.

Mosquito No. 5 (Set 2) was made to sting subject F on two separate days; the first time 25 and the second 27 days after reaching the adult stage, 3 and 5 days, respectively, later than in the positive case reported by the French workers as shown in Table 4.

TABLE 4.—*Inoculations with mosquito No. 5.*

[Nonimmune is designated by a capital letter.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
No. 5.....	F	25-27	No. 5.....	F	27-29

Mosquito No. 6 (Set 3, Group I) was made to sting at age periods of 2, 4, 6, 9, and 12 days longer than in the successful case reported by Marchoux and Simond. In all, five subjects were used.

TABLE 5.—*Inoculation with mosquito No. 6.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
No. 6.....	F	24	No. 6.....	J	31
No. 6.....	G	26	No. 6.....	M	34
No. 6.....	H	28			

Mosquitoes Nos. 7, 8, and 9 (Set 3, Group II) were made to sting subjects B and F. Subject B was stung by all three insects 3 (to 5) days after completing their metamorphoses. Subject F was stung by

insect No. 9 on the twenty-fifth (to twenty-seventh) and again on the twenty-seventh (to twenty-ninth) day after its metamorphosis.

TABLE 6.—*Inoculation with mosquitoes Nos. 7, 8, and 9.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
Nos. 7, 8, and 9.....	B	3-5	No. 9.....	F	27-29
No. 9.....	F	25-27			

Mosquito No. 10 (Set 3, Group III) stung subjects B and G, 2 and 26 days respectively after emergence from the pupal shell, the latter inoculation being 4 days after the 22-day period.

TABLE 7.—*Inoculation with mosquito No. 10.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
No. 10.....	B	2	No. 10.....	G	26

With mosquitoes Nos. 11, 12, 13, and 14 we made one inoculation at least 22 days after completing their metamorphoses, and nine inoculations of seven subjects (B, F, G, J, L, M, and N) at varying intervals after this period up to and including the fortieth day after attaining the adult stage, as shown in Table 8.

TABLE 8.—*Inoculation with mosquitoes Nos. 11, 12, 13, and 14.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		<i>Days.</i>			<i>Days.</i>
Nos. 11 and 12.....	H	22-27	No. 11.....	F	32-37
Nos. 13 and 14.....	J	23-28	No. 12.....	B	32-37
Nos. 11 and 12.....	J	25-30	Nos. 12, 13, and 14.....	G	34-39
No. 13.....	G	25-30	No. 12 and 13.....	J	36-41
No. 14.....	^a L	26-31	Nos. 13 and 14.....	N	39-44
Nos. 12, 13, and 14.....	^b M	30-35	No. 12.....	N	40-45

^a Subject passed from observation after 6 days.

^b Subject passed from observation after 5 days.

We have recorded above our work with particular reference to the mosquitoes. Below (Table 9) we tabulate it with reference to the non-immunes who were the subjects of the inoculations.

until March 2. At this date, 14 days after the metamorphosis, of these *Stegomyia* stung subject A, a Portuguese, who had arrived in Brazil a few days before, and had up to that time never had yellow fever. The subject showed no reaction following this inoculation.

He was stung again by one of these two mosquitoes (the second of which died in the meantime) on the 10th of March, 8 days after the inoculation. Four days later, March 14, he developed a typical mild attack of yellow fever. The character of the period of incubation, the vomiting, the pains, the course of the temperature, the duration, and the progress of convalescence permitted no doubt as to the nature of the disease.

We deemed it a duty, nevertheless, to confirm our diagnosis experimentally. After recovering, this subject was twice submitted to the bites of several *Stegomyia* infected by a case of yellow fever. He proved himself absolutely refractory to these inoculations, as do all individuals recently immunized by a first attack.

It must be added that the conditions under which he was observed by us at the time of his arrival in Brazil do not permit that any source of contamination, other than the hereditarily infected mosquito by which he had been stung, could have brought on the attack of yellow fever which he had presented.

It may be concluded from this experiment that under conditions which can not as yet be precisely defined the *Stegomyia fasciata*, the progeny of a mother directly infected by a case of yellow fever, are themselves infected hereditarily. It follows from the various experiments done on this subject that the time needed by the mosquito hereditarily infected to become capable of discharging the virus with its salivary secretion is longer than in the case of the mosquito which has taken the virus directly from the blood of a patient. This period was 22 days in the positive case.

It follows likewise, both from experiments and from epidemiologic data, that this hereditary transmission can not be considered as the general rule but rather as an exceptional occurrence.

The mildness of the attack suffered by A warrants the belief that the passage of the virus from one generation of *Stegomyia* to another is accompanied by a certain amount of attenuation. This may be a new field open to research with reference to vaccination against yellow fever.

The knowledge of this mode of propagation explains one of the obscure points in the history of yellow fever, that of the recurrence of certain epidemics under conditions where a primary case can not be found that is sufficiently recent to explain the infection of the *Stegomyia*.

Finally, its importance can not be disregarded from the point of view of prophylaxis.

APPENDIX.^a

THE HEREDITARY TRANSMISSION OF THE VIRUS OF YELLOW FEVER IN THE *STEGOMYIA FASCIATA*.

By E. MARCHOUX and P. L. SIMOND.

Among the new facts concerning yellow fever which we gathered in Brazil there is one the importance of which obliges us to publish at once. It concerns the question of the possibility of the hereditary transmission of the yellow fever virus from mosquito to mosquito.

Since 1903 our attention has been turned to the fact that in certain foci of an epidemic zone it is at times difficult to find a case of yellow fever of recent date as the origin of the new cases which spring up at a given time. There being no doubt that the lighting up of these foci was due to the presence of infected *Stegomyia fasciata*, we were forced to conclude that one or several of these mosquitoes had in some way been imported from a distant point where the disease existed from which they had drawn the virus. This undoubtedly occurs frequently. We, nevertheless, were led to ask ourselves if, under certain circumstances, eggs derived from a *Stegomyia* infected in the course of an epidemic some months prior to the one observed could not have given birth to *Stegomyias* hereditarily infected.

Several experiments were made in 1903 to confirm this hypothesis. We had some *Stegomyias* lay eggs that had stung some cases early in the disease. The eggs were hatched into larvæ, and the adult insect raised from these was made to sting a human subject.

These experiments did not give us positive results at that time, although the subjects that had been bitten by these mosquitoes were not immune to the disease, for subsequently it was possible to give it to them by injections of fresh virulent serum.

We resumed these experiments in February, 1905. We collected a number of eggs of one laying from a *Stegomyia* 20 days old which had stung several of our cases in order to determine a heavy infection, and the larvæ which were hatched the 4th of February were placed in a jar to be reared. The adult insects began to emerge February 16. These, isolated in tubes from the time of emergence, were fed with

^a Translated from Comptes Rendus, Société Biologie, Paris, Vol. LIX, No. 27. August 4, 1905, p. 259.

sirup until March 2. At this date, 14 days after the metamorphosis, two of these *Stegomyia* stung subject A, a Portuguese, who had arrived in Brazil a few days before, and had up to that time never had yellow fever. The subject showed no reaction following this inoculation.

He was stung again by one of these two mosquitoes (the second having died in the meantime) on the 10th of March, 8 days after the first inoculation. Four days later, March 14, he developed a typical though mild attack of yellow fever. The character of the period of invasion, the vomiting, the pains, the course of the temperature, the icterus, and the progress of convalescence permitted no doubt as to the nature of the disease.

We deemed it a duty, nevertheless, to confirm our diagnosis experimentally. After recovering, this subject was twice submitted to the stings of several *Stegomyia* infected by a case of yellow fever. He showed himself absolutely refractory to these inoculations, as do all individuals recently immunized by a first attack.

Let us add that the conditions under which he was observed by us from the time of his arrival in Brazil do not permit that any source of contamination, other than the hereditarily infected mosquito by which he had been stung, could have brought on the attack of yellow fever which he had presented.

It may be concluded from this experiment that under conditions which can not as yet be precisely defined the *Stegomyia fasciata*, the progeny of a mother directly infected by a case of yellow fever, are themselves infected hereditarily. It follows from the various experiments done on this subject that the time needed by the mosquito hereditarily infected to become capable of discharging the virus with its salivary secretion is longer than in the case of the mosquito which has drawn the virus directly from the blood of a patient. This period was 22 days in the positive case.

It follows likewise, both from experiments and from epidemiologic facts, that this hereditary transmission can not be considered as the general rule but rather as an exceptional occurrence.

The mildness of the attack suffered by A warrants the belief that the passage of the virus from one generation of *Stegomyia* to another is accompanied by a certain amount of attenuation. This may be a new field open to research with reference to vaccination against yellow fever.

The knowledge of this mode of propagation explains one of the most obscure points in the history of yellow fever, that of the recurrence of certain epidemics under conditions where a primary case can not be found that is sufficiently recent to explain the infection of the *Stegomyia*.

Finally, its importance can not be disregarded from the point of view of prophylaxis.

YELLOW FEVER INSTITUTE, BULLETIN No. 16

Treasury Department, U. S. Public Health and Marine-Hospital Service

WALTER WYMAN, *Surgeon-General*

YELLOW FEVER

ETIOLOGY, SYMPTOMS
AND DIAGNOSIS

BY

JOSEPH GOLDBERGER

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before has fed on the blood of a person sick with this disease during the first 3 days of his illness.

2. That yellow fever can be produced under artificial conditions by the subcutaneous injection of blood taken from the general circulation of a person sick with this disease during the first 3 days of his illness.

3. That yellow fever is not conveyed by fomites.

4. That the *Bacillus icteroides* Sanarelli stands in no causative relation to yellow fever.

As all preventive measures are based on the foregoing fundamental propositions, a somewhat more detailed consideration of each is desirable.

A.—*Yellow fever is transmitted, under natural conditions, only by the bite of a mosquito (Stegomyia calopus) that at least 12 days before has fed on the blood of a person sick with this disease during the first three days of his illness.*

The unusual prevalence of insects during some epidemics of yellow fever was noted more than a century ago. It was not until 1848, however, that any suggestion was made as to their etiological connection. In that year Josiah C. Nott of Mobile, Ala., reasoning from certain epidemic peculiarities of the disease, expressed it as "probable that yellow fever is caused by an insect or animalcule bred on the ground," and mentioned "mosquitoes, flying ants, many of the aphides" as illustrations of insects whose general habits were such as to fulfill the requirements as transmitters of the disease. At about this time there appears to have prevailed a fairly widespread belief in the existence of some relation between mosquitoes and yellow fever, for Dowler, writing in 1855, states that many persons regarded "any increase in the number of mosquitoes as a certain prelude or precursor to a yellow-fever epidemic."

The first to definitely assert that the mosquito is the medium of transmission and to specifically indicate the mosquito concerned was Carlos J. Finlay. In 1881, at a meeting of the Royal Academy of Medical and Physical Sciences of Habana, he stated that three conditions were necessary for the propagation of yellow fever, namely: "(1) The existence of a yellow fever patient into whose capillaries the mosquito is able to drive its sting and to impregnate it with the virulent particles, at an appropriate stage of the disease. (2) That the life of the mosquito be spared after its bite upon the patient until it has a chance of biting the person in whom the disease is to be reproduced. (3) The coincidence that some of the persons whom the same mosquito happens to bite thereafter shall be susceptible of contracting the disease." During the succeeding twenty years Finlay continued, tenaciously, to

maintain his theory which, in collaboration with Delgado, he attempted, though unsuccessfully, to prove.

To Reed, Carroll, Agramonte, and Lazear is due the credit for the masterly experiments which converted a discredited hypothesis into an established doctrine.

The transmission of the disease by the mosquito is not, as Finlay thought, a simple mechanical transfer from one individual to another, such as occurs at times in plague through the instrumentality of fleas or in surra through biting flies. In these diseases neither the flea nor the fly is necessary, but in yellow fever not only is the mosquito necessary, but it is essential that the mosquito be of a particular species or at least of a particular genus. Thus, attempts to transmit the disease by means of mosquitoes of other than the genus *Stegomyia*^a have not been successful.

It has been found, furthermore, that in yellow fever, unlike either surra or sleeping sickness, a certain period must elapse after the infecting feed before the mosquito is capable of communicating the disease.^b Experimentally this interval appears to be not less than 12^c days, so that a susceptible individual may expose himself with impunity to repeated stings within the first 10 or (?) 11 days^d after the mosquito has fed on a person sick with the disease. This is the period of "extrinsic incubation" of Carter, whose painstaking observations at Orwood and Taylor, Miss., in 1898, resulted in his tentatively fixing this interval as "usually in excess of 10 days" and served, in the light of the then recent discovery of the mosquito transmission of malaria, to direct the attention of the Army Commission to Finlay's mosquito as a possible "intermediary host" for this disease.

The duration of this period of "extrinsic incubation" is decidedly influenced by the temperature of the air. It is at its minimum at temperatures above 26° C (80° F), but becomes progressively longer as the temperature declines below this point.

The period of the disease at which the mosquito bites is another essential factor in the latter's power to transmit the disease. Thus all attempts to produce an attack by means of the bites of mosquitoes that had previously fed on cases after the third day of the

^a No experiments have as yet been recorded with any species of this genus other than *S. calopus*.

^b In surra and sleeping sickness for example, no such interval exists. On the contrary, it is only during the two days immediately following the infecting feed that the tsetse flies concerned can transmit these diseases. After the third day their bite is perfectly harmless. In dengue this interval appears likewise to be absent.

^c I say "appears to be," because the recorded experimental evidence is not sufficient to prove that it may not under favorable conditions be a (very) little shorter than 12 days.

^d Nor do such bites during this period confer, as Finlay believed, an immunity from subsequent attack.

disease have failed,^a whereas all successful attempts have been with such mosquitoes as had been allowed to feed on cases during the first three days.

There are some who, while granting that the mosquito is capable of transmitting the disease directly by biting, maintain that the disease may also be acquired by ingesting water in which the body of an infected mosquito has disintegrated. Again, there are others who, while admitting that the mosquito is the sole medium of transmission, hold, nevertheless, that there may be sources other than the one mentioned from which this insect may acquire its infection, and suggest black vomit or articles soiled by yellow-fever patients as pertinent illustrations. But neither the results of experiments especially designed to test these hypotheses nor the indirect evidence furnished by a large mass of observations give the slightest support to these assumptions. After the mosquito has become infective it probably remains so for life.

B.—*Yellow fever can be produced under artificial conditions by the subcutaneous injection of blood taken from the general circulation of a person sick with this disease during the first 3 days of his illness.*

The subcutaneous injection of a drop^b (0.1 cc.) of yellow fever blood serum from a case in the first day of illness has produced an attack of yellow fever, whereas five times this amount from a case in the fourth day of the disease produced no symptoms.

C.—*Yellow fever is not conveyed by fomites.*

Before the demonstration by the Army Commission of the transmission of yellow fever through the mosquito it was very generally believed, notwithstanding a large mass of evidence to the contrary, that the disease was communicated by the exhalations of the sick, by contact with their excretions, or with articles that had been exposed to or been soiled by them.

In order to put this almost universal belief in fomites to a rigorous test, the Army Commission exposed each of a series of seven non-immunes to clothing and bedding which had been used by cases of yellow fever and which had become soiled with blood, urine, feces, and black vomit. The house in which the experiment was carried out was especially constructed for the purpose in an isolated place near Habana. In order to prevent access of mosquitos and to simu-

^a The recorded experimental evidence is not sufficient to show that this infective period may not at times extend into the fourth day. This is of considerable practical importance. A case of yellow fever should be protected from mosquitoes during four full days at least.

^b Parker, Beyer, and Pothier (1903) induced an attack of yellow fever by the subcutaneous injection of 0.033 cc. of filtered serum from a case in the third day.

late the conditions thought most favorable to infection by fomites, the windows and doors were screened and so placed as to prevent free ventilation, special pains were taken to exclude sunlight, and provision was made for heating during the day so that an average temperature of 72.6° F. was maintained throughout the entire period. The men were exposed in squads for periods averaging 21 nights each. Each squad entered the house at night, removed the soiled articles from the boxes in which they were packed, shook them out, hung some about the room, and used some for making up the beds in which they slept. In the morning the various garments and articles of bedding were repacked and the men left the room to occupy a near-by tent during the day. The result of this experiment was entirely negative; the men remained in perfect health. Subsequently some of them submitted to mosquito inoculation and promptly sickened with the disease, showing conclusively that they were not immune.

It may be of interest to observe that the first experiments to determine the infective power of fomites were made over a century ago. In 1800 Cathrall reported having repeatedly applied black vomit to his tongue and lips and to the skin of various parts of the body without experiencing any ill effects. In company with a friend he had, besides, exposed himself to the fumes of heated black vomit, both in the open air and in a confined space, likewise without harm. In 1804 Ffirth, imitating Cathrall's example, went so far as to repeatedly swallow several ounces of fresh black vomit; he rubbed some into incisions in his arms and dropped some into his eye without experiencing any but momentary disagreeable effects.

In view of the foregoing, one can not but admire the acute reasoning of La Roche,^a who, half a century ago, in discussing the evidence in support of transmission through the agency of clothes, bedding, merchandise, etc., concluded that "we may well infer" that in the record of such instances "some error has crept in—something has been omitted or overlooked—and that the production of the disease was really due to some other agency than the one contended for," a conclusion which will be concurred in by anyone who will take the pains to critically examine the recorded instances of alleged transmission by such means.

D.—*Experiments to show that the Bacillus icteroides Sanarelli stands in no causative relation to yellow fever.*

The fact that the Army Commission was able to produce three cases of yellow fever by the subcutaneous injection of blood which was shown to be sterile by the culture method is sufficient to eliminate

^a Vol. 2, p. 522.

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100

inferred that the parasite is one of those that requires for the complete evolution of its life cycle a mammalian and an arthropod host. We have familiar analogies in *Piroplasma bigeminum* of Texas fever and the *Plasmodium* of malaria. Because of these analogies it is inferred that biologically it may be grouped with them as a protozoon. On the basis of these and other analogies, both Schaudinn (1904) and Novy & Knapp (1906) have suggested that it may be a *Spirochæta*. Stimson's recent discovery of a spirochæte-like organism in the tubules of a yellow fever kidney is, therefore, exceedingly interesting and suggestive.

The cycle in man is represented clinically by a stage of incubation and by a stage of fever. Some attempts to infect mosquitoes by allowing them to bite subjects during the stage of incubation, in one instance as late as 6 hours before the onset of the stage of fever, have been unsuccessful; whereas a mosquito that bit a case of the disease 8 hours after the onset became infected and conveyed the disease to a nonimmune 26 days later. This would indicate that the parasite does not appear in the circulating blood until the onset of the disease. We already know that it remains in the blood only during the first three days of the disease or, at least, it is only during those three days that it exists in a form capable of continuing its life cycle in the mosquito or in a fresh nonimmune.

In the circulation it exists in a form so minute as to be capable of passing through the finest grained porcelain filters, such as the Chamberland B and the Chamberland F.

Its resistance to deleterious influences is feeble when withdrawn from the circulation. When kept in a test tube exposed to the air in the dark, at a temperature of 24° C. (75° F.) to 30° C. (80° F.), it loses its virulence in 48 hours. Under the same conditions, but protected from the air by keeping under oil, it retains its vitality somewhat longer—up to between 5 and 8 days. Heating for 5 minutes at 55° C. (132° F.) apparently suffices to kill it. The effect of low temperatures has not been studied.

The cycle in the mosquito requires at least 12 (?) days^a for its completion. As to the changes which it undergoes during this period we are in complete ignorance.

The French commission has recorded one experiment which would indicate that the parasite may, under certain circumstances, be transmitted to the progeny of an infected mosquito through the egg. An attempt by Rosenau and Goldberger to confirm this resulted negatively. The same commission attempted, but without success, to transmit the parasite from one mosquito to another by feeding larvæ with cadavers of infected adults; they appear, however, to have succeeded in trans-

^a See page 5, footnote c.

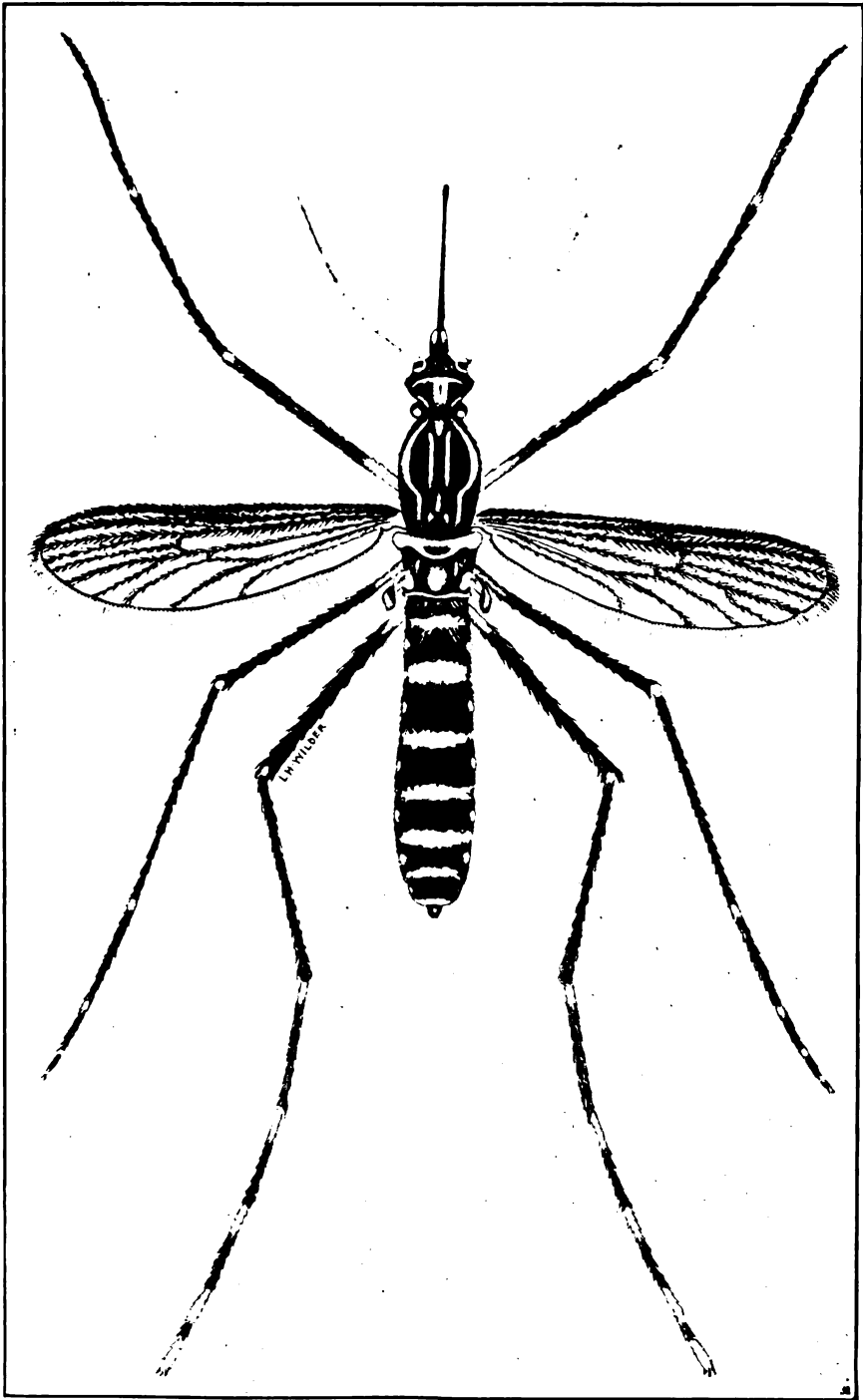


FIG. 2.—*Stegomyia calopus* (female).

between the male and the female is readily discernible in the characters of the antennæ; in the former (fig. 3) these organs are prominent and feathery—decidedly hirsute. Another prominent point of difference exists in the length of the palpi; in the male they are long—almost as long as the proboscis, but in the female they are short—less than one-third the length of the proboscis.

The palpi in both sexes are black, but are ornamented with white scales which, in the male, are arranged as four narrow bands, while in the female they are collected into a white tuft at the tip.

The proboscis is black and is devoid of ornamentation, differing in this respect from both *Culex teniorhynchus* and *Culex sollicitans*, each of which has the proboscis marked by a pale band in the middle. These two insects bear a superficial resemblance to *S. calopus*, for which they are not infrequently mistaken by the uninformed.

The head is clothed by the broad flat scales characteristic of the genus. These scales are black, except for a line of white down the middle extending to the neck and a narrow white border to the eyes.

The thorax is dark brown, almost black, ornamented with silvery white patches and lines of which the following are peculiar to and distinctive of this species, and enable one to recognize it at a glance: A well marked, easily recognizable, pure white curved line on either side of the back (mesonotum) between which, but less obvious to the naked eye, are two delicate median parallel lines; a prominent transverse white line of scales on the scutellum.

The abdomen is clothed with black and white scales, the latter collected in bands at the bases of the abdominal segments, and in distinct patches at the sides.

The legs are black scaled, except for white bands which are arranged as follows: A basal band on the first joint of the fore, on the first and second of the mid, and on all of the hind tarsi except the last, which is, as a rule, all white. Each leg is provided with a pair of claws which are equal in size in the female but unequal in the male. They differ in other respects in the two sexes; in the female those of the fore and of the mid legs are provided with one tooth, those of the hind legs are simple; in the male all the claws are simple except the larger one of the forefoot.



FIG. 3.—Appendages of head of *Stegomyia calopus* (male).

The veins of the wings are clothed with dark brown scales. The first submarginal cell is longer than the second posterior cell and the base of the former is nearer the root of the wing.

Biting.—The male insect does not bite; it lives almost exclusively on vegetable and fruit juices. In the females, however, a feed of blood is a necessary condition precedent to egg laying. At summer temperatures this insect will digest a full meal of blood in about 48 hours. If disturbed in the act of feeding it will fly away, but will return and attempt to finish its interrupted meal. In this way one infected mosquito in its efforts to obtain one full meal may bite several individuals, and so may, almost simultaneously, produce more than one case of yellow fever.

It has long been observed that communication with an infected town is distinctly safer during the day than after dark. In an effort to explain this phenomenon the French yellow fever commission first suggested, then made some experiments which appear to show that under natural conditions the yellow fever mosquito, after the first week, ceases to bite during the day and bites only at night—that is, between 5 p. m. and 7 a. m. These results are not, however, altogether in harmony with the observations of others, and there are cases recorded showing that yellow fever may be contracted by visiting an infected house during the day.^a We must conclude, therefore, that the *Stegomyia calopus*, young or old, may bite at any time during the 24 hours, though probably it is most vicious about dusk and about dawn. The female is impregnated almost immediately after her birth, and then proceeds to seek a blood feed; 3 or 4 days after this she is ready to lay her eggs.

Breeding places.—The *Stegomyia calopus* appears to be strictly a house mosquito—a domestic though not domesticated animal. Her breeding places, therefore, may be expected, and actually have been found to be any collections of water in and about habitations, such as cisterns, wells, water barrels, tubs or jars with or without water plants, sagging roof gutters, more or less broken and discarded crockery, bottles and tins, fountains (not containing fish), cemetery vases, baptismal and other fonts in churches, chicken or horse troughs, grindstone troughs, and tubs or barrels containing water which has been softened and made more or less alkaline by the use of ashes. The larvæ have been found in tin cans containing fecal matter, in cesspools, and in some natural collections of water formed by leaves of certain tropical plants, such as the palm and century plant. Ordinarily, she does not seek street puddles or gutters, favorite breeding places for *Culex tæniorhynchus* and *Culex pipiens* (= *pungens*), though her larvæ have been found in these situations.

^a Carter, 1901b, p. 936.

Egg.—The female lays her eggs (fig. 4) on the surface of the water or on the sides of the container at or just above the water line. The eggs do not adhere one to the other to form the compact boat-shaped masses characteristic of *Culex* (fig. 5), but lie on their sides more or less isolated, though frequently grouped into clumps. At the moment of laying the eggs are of a cream color but rapidly become jet black; they are somewhat cigar shaped with one end slightly broader and more bluntly rounded than the other. They measure on an average about 0.55 mm. in length and 0.16 mm. in width at the broadest part. Under the microscope the apparently cylindrical egg is seen to be slightly flattened on one side. The eggs are most commonly laid during the night or early morning, but they may be laid at any time during the 24 hours. The total number of eggs laid varies, the average being about 65 to 70; the maximum recorded is 144.^a



FIG. 4.—Eggs of *Stegomyia calopus* (after Stephens & Christopher, 1904).

The act of ovipositing appears to greatly exhaust the mosquito, so that it may fall on the surface of the water and die immediately after even the first egg laying. There are numerous exceptions, however,

and the act may be repeated several times and the mosquito survive for some time after.

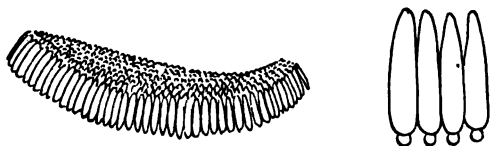


FIG. 5.—Eggraft and eggs of *Culex* (after Stephens & Christopher, 1904).

If laid on the surface of the water the egg floats, being supported by the surface film. Disturbance of the water surface may

cause the egg to become wet and sink to the bottom, but this does not prevent its hatching out into the larva. The egg shows marked powers of resistance to unfavorable influences. Thus it may be kept dry for from two or three to six and one-half months^b and still retain its vitality and hatch out when put back into the water. Reed and Carroll^c have shown that freezing does not destroy its vitality. The egg probably plays the leading rôle in the hibernation of this mosquito.

Under the most favorable conditions as to temperature (30° C. (86° F.) and over) eggs hatch out in about 36 hours after they are laid, but with a lowering of the temperature this period becomes progressively longer until 20° C. (68° F.) is reached, below which they will not hatch at all.

^a Marchoux and Simond, 1906b. ^b Francis, 1907. ^c Reed and Carroll, 1901.

Larva.—The egg hatches into the larva ("wiggle-tail") (fig. 6), which can be distinguished readily from the larva of *Culex pipiens* (fig. 7), its most common messmate, by the color and proportions of the breathing siphon (air tube). In the *S. calopus* the respiratory siphon is black and somewhat barrel-shaped, with its greatest transverse diameter equal to about one-half of the length; whereas in *Culex pipiens* the air tube is brown, longer, more slender, and with the greatest transverse diameter less than one-third of the length of the tube. The larva, though it lives in the water, is strictly an air breather and must come to the

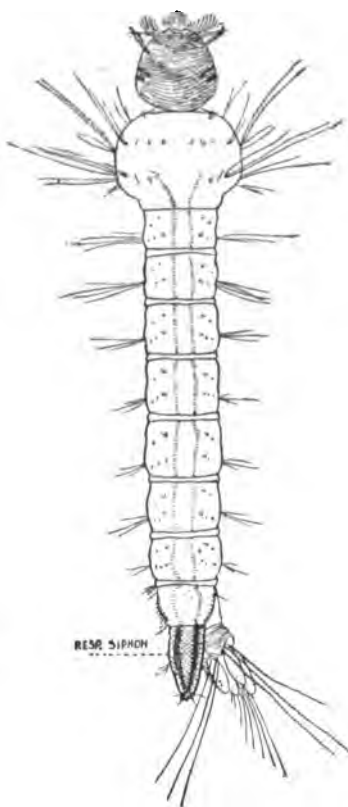


FIG. 6.—Larva of *Stegomyia calopus* (after Howard, 1901).

surface for air. It thrusts its breathing tube up into the surface film and remains suspended head down, at an angle somewhat less than 45° , for a variable time. A film of oil on the surface of the water is sufficient to obstruct the air tube, and thus cause the death of the larva by suffocation. The larva is very timid, so that a very slight jar or a sudden shadow will cause it to move rapidly to the bottom of the container where, indeed, it may very commonly be observed to feed.

The duration of the larval stage is influenced by food supply and temperature. With an abundant supply of food and under favorable

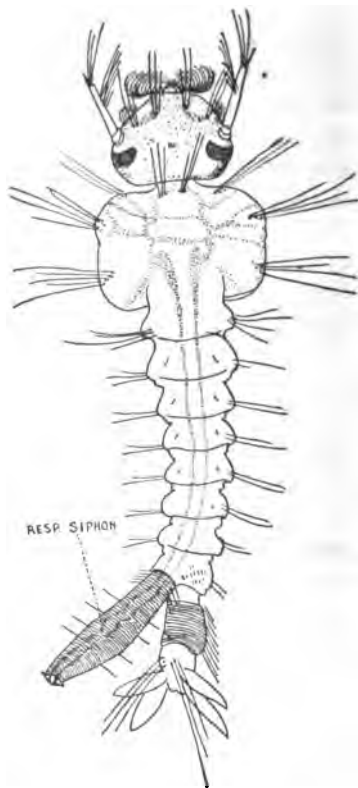


FIG. 7.—Larva of *Culex pungens* (after Howard, 1901).

conditions of temperature this stage lasts not less than 6 or 7 days; under conditions where the supply of food is scanty or the temperature reduced the duration of this stage may become very much prolonged (weeks) or development may altogether cease. In the latter case the larva may die without completing its metamorphosis or, with the return of favorable conditions, it resumes its development. Freezing for short periods does not appear to injure it.

Pupa.—After several moults the larva changes into the pupa (fig. 8). The pupa is not provided with a mouth and does not feed. It spends its time at the surface of the water for, like the larva, it is an air breather, and is provided with two trumpet-shaped breathing tubes which spring, not from the tail as in the larva, but from the dorsum of the thorax. It moves only when disturbed, and then rather rapidly and jerkily downwards into the depths. The pupal stage lasts at least 36 hours, during which time important changes take place in its internal organization preparatory to the emergence of the perfect insect or imago. The pupal, like the larval stage, is normally passed in the water. Berry has shown, however, that the pupa may be spilled on the ground without its metamorphosis being interfered with. Under the most favorable conditions it takes at least 9 days from the time the egg is laid to the appearance of the imago.

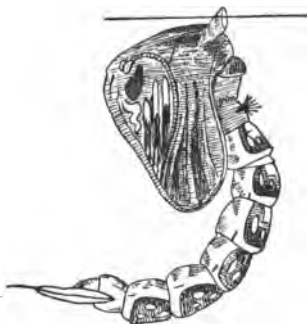


FIG. 8.—Pupa of *Stegomyia calopus* (after Howard, 1901).

Longevity.—The length of life of the adult female under natural conditions probably varies greatly. Experimentally, Guiteras (1904a) succeeded in keeping a presumably infected one alive for 154 days at the fall and winter temperatures of Habana. At summer temperatures, deprived of water, it does not usually survive longer than $3\frac{1}{2}$ to 4 days, and only very exceptionally 5 days. This fact has a bearing on the possibility of transporting the mosquito in handboxes or trunks.

Its activity, which is greatest at about 30°C . (86°F .), distinctly diminishes as the temperature declines and approaches 20°C . (68°F .). Below the latter point and as the temperature of 15°C . (59°F .) is approximated the insect seeks obscure corners for protection, becomes very sluggish, and can only exceptionally be induced to bite. In a refrigerator at 8° to 10°C . (46.5° to 50°F .) Guiteras (1904a) was able to keep some mosquitoes alive without food or water for 87 days. How much longer they may have lived it is impossible to say, because the experiment was terminated at the end of this time by some ants that gained access to and destroyed the mosquitoes. A freezing temperature kills the mosquito rather quickly.

In the influence of variations in temperature on the rate of multiplication, on the activity and on the duration of life of the mosquito we have a satisfactory explanation of the peculiarities of seasonal prevalence of the disease in endemic foci, of the decline of epidemics with the advent of cool weather, and of their abrupt cessation on the occurrence of a severe frost. The occurrence of cases even after a killing frost is explained by the fact, already mentioned, that the *S. calopus* is peculiarly a house mosquito, and it is for this reason occasionally able to escape the full rigors of the climate.

Aërial conveyance.—On this subject I can do no better than quote Carter (1904), who has given it a great deal of attention.

Although direct observations on this problem are few, yet there are certain indirect ones bearing, however, entirely on the aërial conveyance of the *Stegomyia* infected with yellow fever. It is notorious that yellow fever is usually conveyed but a short ways aërially "across the street" or more often "to the house in the rear," which is about as far as it was expected to be thus conveyed. This represents a distance of about 75 yards. The two longest distances recorded in recent times of aërial conveyance, one of 225 meters (Melier) and one of 76 fathoms—456 feet (the writer)—are entirely exceptional. So much for the distance which the "infected" *Stegomyia* is conveyed—or, rather, usually conveyed—aërially.

On the other hand, it is known that vessels moored in certain districts of the Habana harbor did not develop yellow fever aboard except in those who had been ashore or unless they lay close to other vessels which were infected. This experiment has been made on so large a scale, with so many vessels, and for so many years that we must accept as a fact that an infected *Stegomyia* was not conveyed aërially from the Habana shore to those vessels, or, allowing for errors, was very rarely so conveyed. The distance which had been found safe was something over 200 fathoms—1,200 feet. The prevailing wind was generally slightly on shore, but was not constantly blowing. Whether there is any difference in the distance to which infected or noninfected mosquitoes are conveyed is, of course, entirely a matter of surmise. There is no apparent reason why there should be. Yet the infected *Stegomyia* have almost certainly become so in a house, and with their very domestic habits must be found out of doors, where they would be subject to conveyance by the wind in much smaller numbers than the uninfected insects, and consequently a lesser number of them would be conveyed aërially. Observation is needed on this subject—the distance (across water) that *Stegomyia* are aërially conveyed.

Conveyance by railroads and vessels.—The yellow fever mosquito may be conveyed from one place to another in the railway car. I captured one in a day coach en route between Donalsonville and Bainbridge, Ga., in August, 1905. My experience in traveling by rail, both in Mexico and in the southern part of the United States, leads me to believe that the number thus conveyed is very small, so that the chance of conveying one that is infected is probably very slight.

Distribution by vessels may not infrequently be observed. They have been found on steam vessels, but much more commonly and in greater numbers on sailing vessels, because the latter are more likely to present easily accessible breeding places. It can hardly be doubted that the outbreaks of yellow fever in such northern cities as Baltimore, Philadelphia, New York, Boston, and Quebec were due to the

importation on sailing vessels of infected mosquitoes. These in proportion as they found conditions favorable, multiplied more or less rapidly and abundantly and produced epidemics which were more or less closely confined to, or in the neighborhood of, the shipping.

Geographic distribution.—The *Stegomyia calopus* has been found to be one of the most widely distributed of mosquitoes. It is primarily a tropical insect, but has extended north and south along lines of travel, establishing itself permanently wherever the conditions of temperature and moisture are favorable. Speaking broadly, it belts the globe between 38° north and 38° south latitude.

Within the United States the points at which it has been found, with few exceptions, "fall within the limits of what are known as the tropical and lower austral zones. These life zones include practically all of the southern United States which border on the Atlantic Ocean and the Gulf of Mexico, with the exception of those portions of Virginia, North and South Carolina, Georgia, and Alabama which constitute practically the foothills of the Appalachian chain; in other words, western Virginia and North Carolina, the extreme northwestern corner of South Carolina, the northern part of Georgia, and the extreme northeastern corner of Alabama. Further than this, the lower austral zone includes the western half of Tennessee, the western corner of Kentucky, the extreme southern tip of Illinois, the southeastern corner of Missouri, and all of Arkansas except the northern portion. It also includes the southern portion of Indian Territory, southern Arizona, and some of northern Arizona, and southern strips in Utah, Nevada, and California.

"In the greater part of the territory thus indicated, and *where the climate is not too dry*, *Stegomyia fasciata* will, with little doubt, upon close search, be found.

"All the rest of the lower austral territory just indicated, and *where the climate is not too dry*, will constitute a region where the yellow-fever mosquito, if once introduced, will undoubtedly flourish. Even in the dryer portions of western Texas, southern New Mexico, southern Arizona, southern California, and southern Nevada, where the climate is exceptionally dry, there is a possibility that this species, if once introduced, will breed in the water supply of ranches, except, possibly, where the water is impregnated with alkali."^a

INCUBATION.

In 29^b cases of experimental yellow fever, recorded in the literature, produced by mosquitoes *in nonimmunes that had not been subjected to*

^a Howard, 1903.

^b This does not include one case apparently induced by mosquitoes that had acquired their infection by feeding on sirup in which the bodies of infected mosquitoes had been crushed. In this case the incubation period would appear to have been not less than 9 nor more than 12 days.

previous inoculations with blood serum, the period of incubation varied from not less than 2 days 1 hour to 6 days 2 hours. In 25 of these cases the incubation period did not exceed 5 days, leaving four cases, or 13.8 per cent of the total, in which this period was in excess of 5 days. There is some reason for believing that this period may, exceptionally perhaps, be prolonged to 8^a or 10^b days.

The limits of variation of this period in the experimental cases produced by blood injection were from 1 day 15 hours to 12 days 18 hours in subjects that had not been subjected to other than the one blood inoculation.

The length of the period of incubation appears to bear no direct relation to the number of mosquitoes used for the inoculation; nor does it appear to bear any direct relation to the age of the insect or insects or to the character (mild or severe) of the case from which they obtained their infection or which they induce.

SYMPTOMS.

Yellow fever is a disease that manifests itself in all grades of severity, from an attack suggesting a "slight attack of grippe" or "indigestion" of such mildness as hardly to interfere with one's daily routine, and not calling for medical attention, to an attack of such malignancy that the physician finds himself powerless to stay its course to a fatal termination. Besides this great difference in the virulence of individual attacks, there is considerable variation in their duration and in the relative prominence of certain symptoms. These differences have been used by different writers in various ways as a basis for dividing the disease into different clinical types. As these divisions are of no practical use they will not be considered.

Onset.—In most cases the transition from a state of well being is abrupt and may be marked by the occurrence of a chill or chilliness, or by the appearance of a severe frontal headache, or pain in the lumbar region of such severity as to suggest an attack of smallpox or, occasionally, in children by the occurrence of convulsions. In these cases close questioning will not infrequently elicit a history of indisposition for perhaps 12 to 24 hours before the occurrence of the symptom or symptoms that definitely mark the onset of the disease. In a smaller proportion of cases the patient takes to his bed in consequence of a rapidly increasing lassitude with or without headache.

The disease may be ushered in at any time during the 24 hours, so that one not infrequently obtains a history of the patient's having been awakened at night by the occurrence of a chill, or awakening in the morning with fever, headache, and nausea.

^a Carter, 1901a, p. 366.

^b Marchoux, Salimbeni and Simond, 1903, p. 674, footnote.

Pains.—Pain in some form is one of the earliest and one of the most constant symptoms. It is usually marked, but at times, in children, and occasionally in mild cases in adults, it may be slight, and in the former sometimes altogether absent. Frequently marking the onset or, if not, appearing soon after, are headache, pain in the back and limbs. After two or three days, with the decline in the fever, the severity of these usually diminishes. The headache is usually frontal, but it is sometimes temporal or occipital; there is usually associated with it more or less aching of the eyes. The pain in the back is sometimes described as if it had been produced by blows with a rod, on which account the French in the West Indies have called it the *coup de barre*; in some instances it is not unlike the lumbar pain of smallpox. The aching in the limbs has its seat in the muscles, and affects more particularly the muscles of the thighs and calves of the legs.

Facies.—With the onset of the disease the face usually becomes flushed and somewhat swollen. The flushing may be slight or occasionally altogether absent, or it may be so marked as to suggest the initial rash of dengue, especially if it extends, as it sometimes does, down the neck to the upper part of the chest. The amount of swelling varies; it may be inappreciable or it may be sufficient to smooth out somewhat the lines of expression. Coincident with the flushing of the face the eyes become congested and red and sensitive to light. In mild cases the injection of the conjunctiva may be shown only as an abnormally prominent capillary mesh; in the severe cases the conjunctiva may appear as if inflamed, and in rare instances it may become raised around the cornea from infiltration of serum and blood. The flushing of the face and the injection of the eyes usually diminish as the temperature begins to decline.

In certain grave cases, coincident with the appearance of black vomit, the face becomes pale, the lips cyanosed, the eyes sunken, and the redness of the conjunctivæ becomes replaced by a more or less distinct tinge of yellow.

Skin.—At first the skin is warm to the touch and usually, but by no means always, dry; sometimes, indeed, it is covered with perspiration which may persist throughout the disease. Later, in some cases, with the occurrence of black vomit, the skin becomes cool and clammy. Jaundice occurs in all but some mild cases; it usually appears first about the third day as a slight tinging of the ocular conjunctiva. At almost the same time, or very soon after, it may be noticed that the skin also has acquired a pale yellow tint. Its early detection may be facilitated by pinching up a fold of skin and causing a momentary local anæmia.

As the case progresses the icteric tint, which at first is faint, gradually becomes more pronounced. The depth of color attained varies

from a pale lemon to an orange or a saffron hue. In some cases the jaundice may appear somewhat earlier than the third day; in others somewhat later, or not until convalescence. In some fatal cases it may not present itself until after death. After convalescence is established the icterus more or less rapidly fades away.

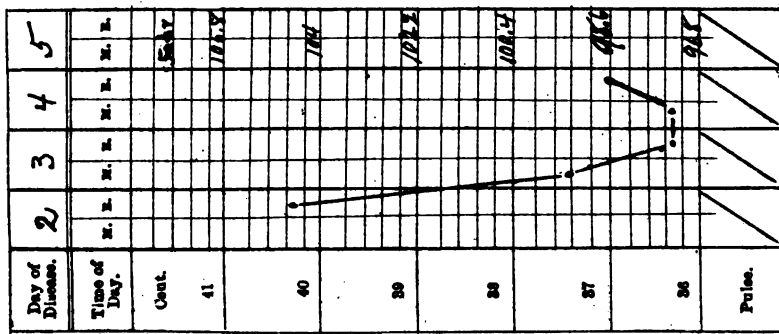
Various accidental eruptions, such as sudamina, herpes, and echymotic patches are occasionally observed.

Odor.—An odor variously described has been noted by many writers. Some have considered the odor so peculiar as to be almost pathognomonic. While I have myself never detected any odor that I could differentiate from that which may occasionally be noted in other diseases, and while I can conceive that as the result of pathological changes volatile odorous matters may be given off by the skin (or lungs) that are peculiar to the disease, I am, nevertheless, constrained to believe that some, at least, of the observers who have noted these “characteristic” odors have deceived themselves, especially when I read that the odor was detected “twelve days before the development of the fever.”

Temperature.—With the onset of the disease the temperature rises and usually continues its ascent for from 24 to 48 hours. During this initial rise the fever frequently reaches the highest point which it attains during the disease. This does not commonly exceed 40.2°C . (104.5°F). A temperature above 41°C . (105.5°F .) is but rarely recorded. Its subsequent course varies considerably, but on scrutiny it will, speaking broadly, conform to either of two general types: In one the fever having reached its acme the temperature declines progressively and more or less rapidly, with or without evening exacerbations until it reaches normal (charts 1, 2, 3, and 4). In the other the temperature continues with more or less marked oscillations for 3, 4, or 5 days at or near the point to which it first rose, and then, more or less rapidly, declines to the normal (charts 10 and 11). The cases which conform to the latter type are usually the more grave and more likely to be fatal; but some of the most rapidly fatal cases (chart 2)—the so-called *foudroyante* cases of the French—belong in the former category.

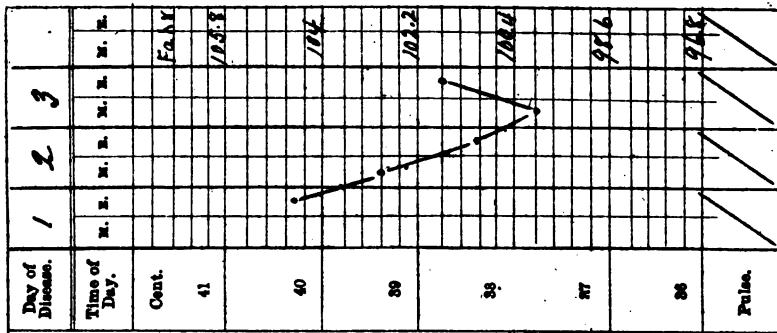
The initial rise is occasionally interrupted by a decided, though short, remission or by a complete intermission which may last 6 to 10 hours. I have seen an intermission lasting at least 6 hours occur 14 hours after the onset (chart 6). Both the remission and the intermission may be, and more commonly are, delayed until the completion of the initial rise and are then, particularly the remission, somewhat more prolonged (charts 5, 7, 8, and 9). The remission may be repeated (without the occurrence of black vomit) so that the temperature curve assumes a distinctly remitting character (charts 8 and 9). A fall in temperature frequently marks the onset of black vomit. It is for this

CHART 1.



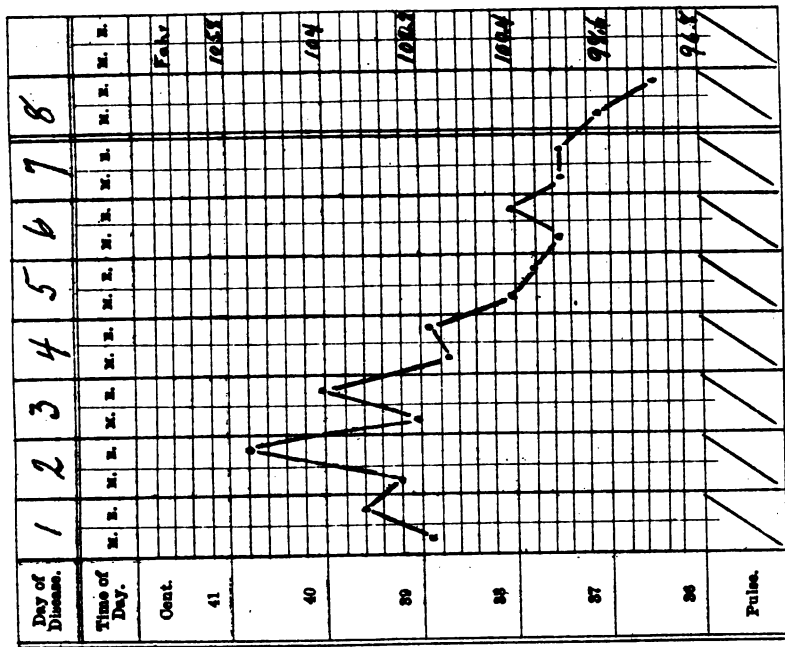
Yellow fever, descending type; very

CHART 2.



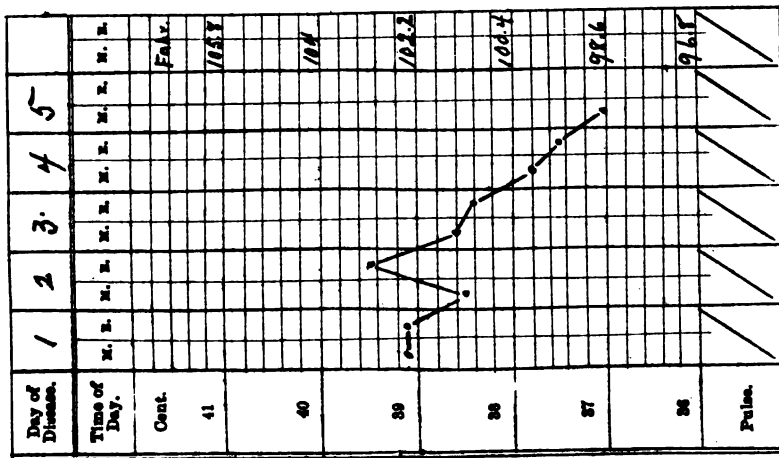
Yellow fever, descending type; fatal in 12 days 20 hours

CHART 4.



Yellow fever, descending type; medium severity; duration, 8 days; recovery.

CHART 3.



Yellow fever, descending type; mild; duration, 5 days; recovery.

CHART 5.

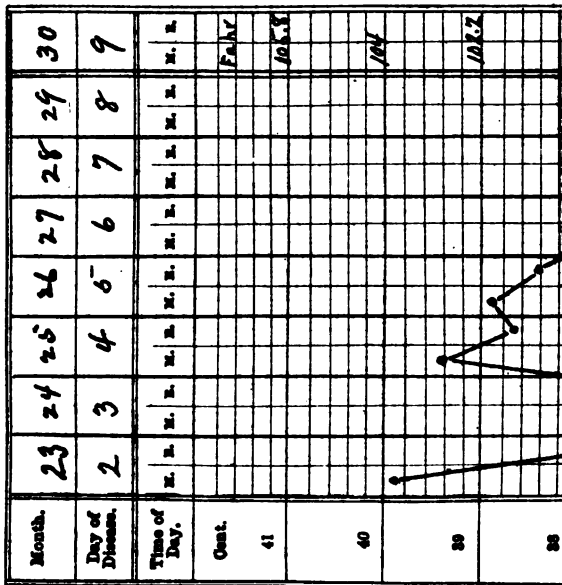
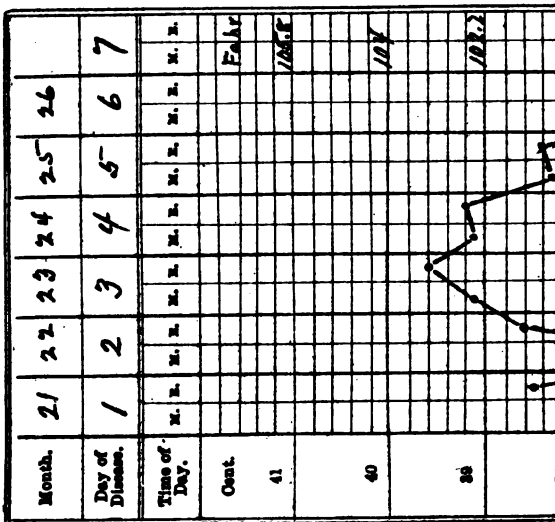


CHART 6.



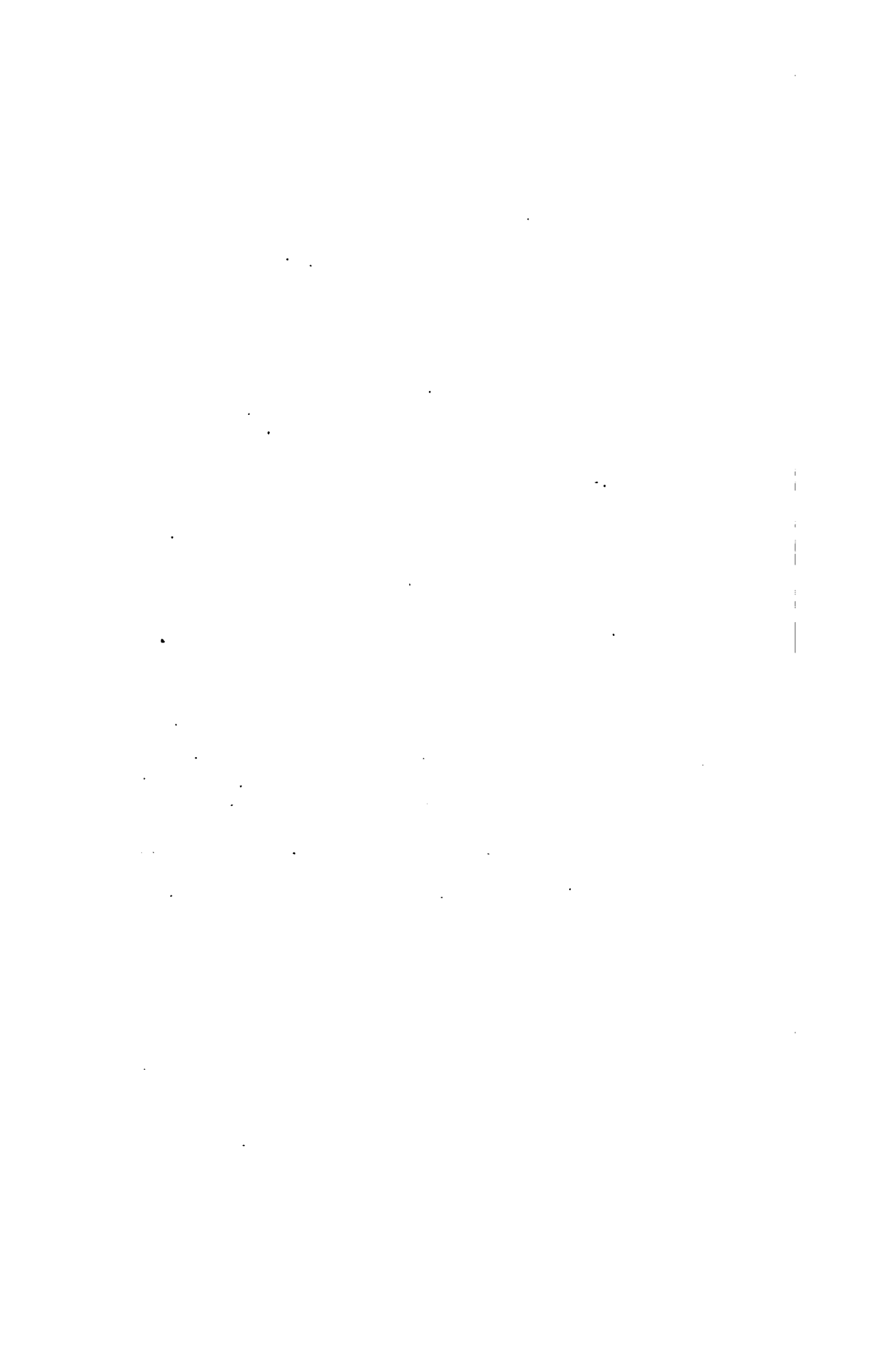
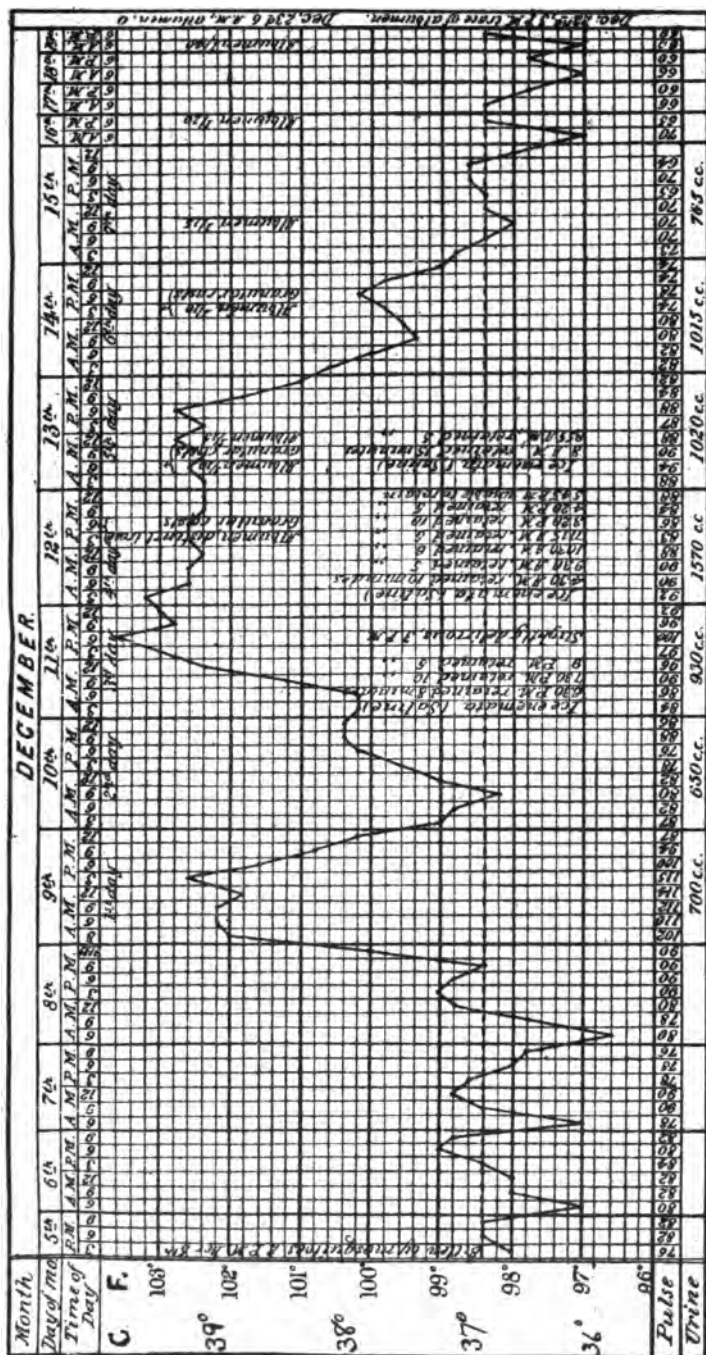
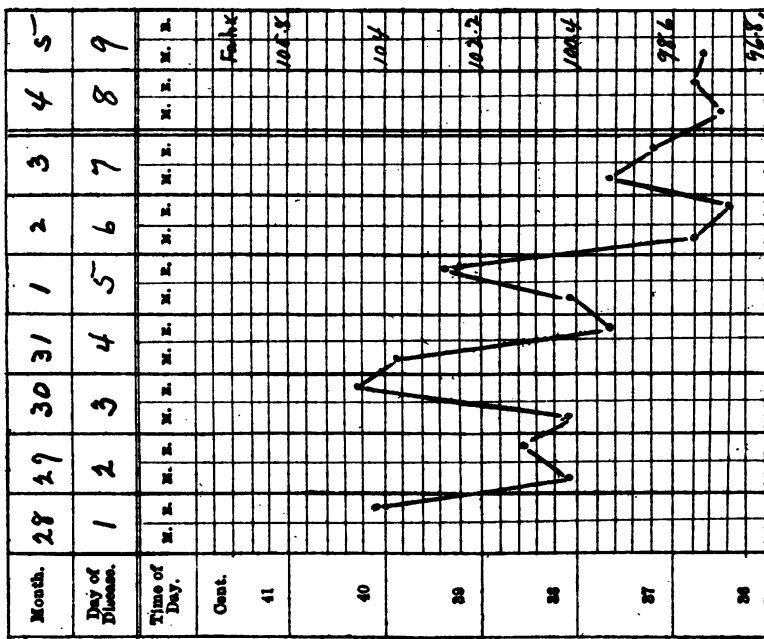


CHART 7.

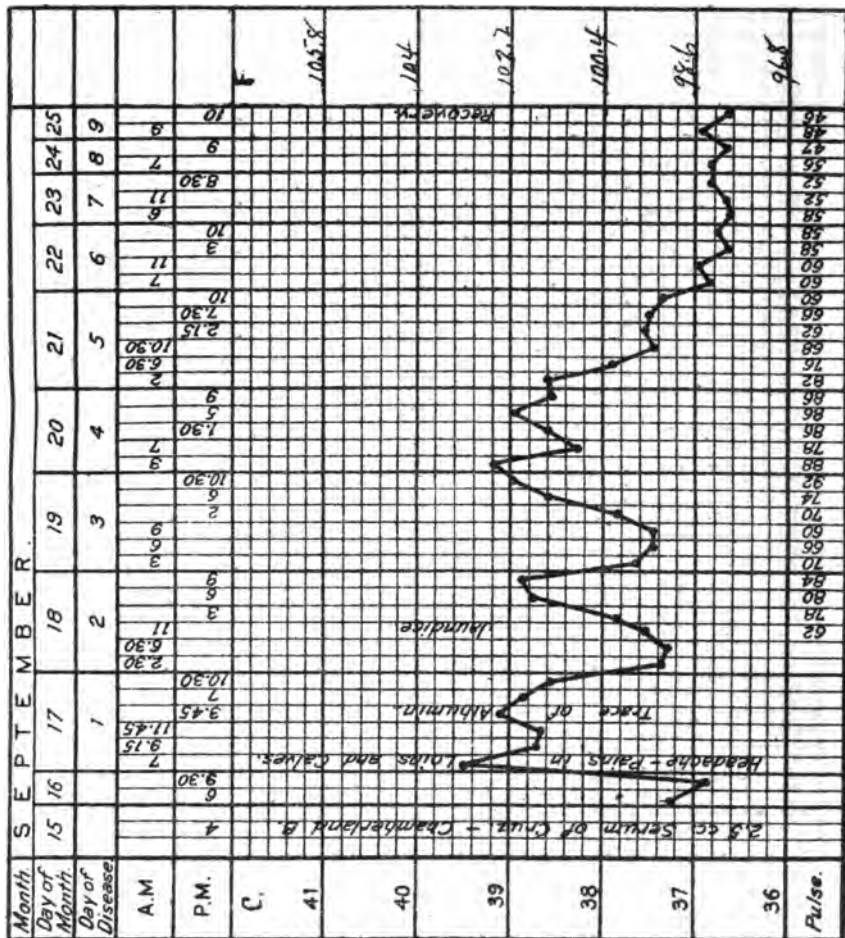


Yellow fever, intermitting type; intermission, 24½ hours after onset. Experimental, by bite of *Stegomyia calopus*. (Reed, Carroll, and Agramonte, 1901.)

CHART 8.

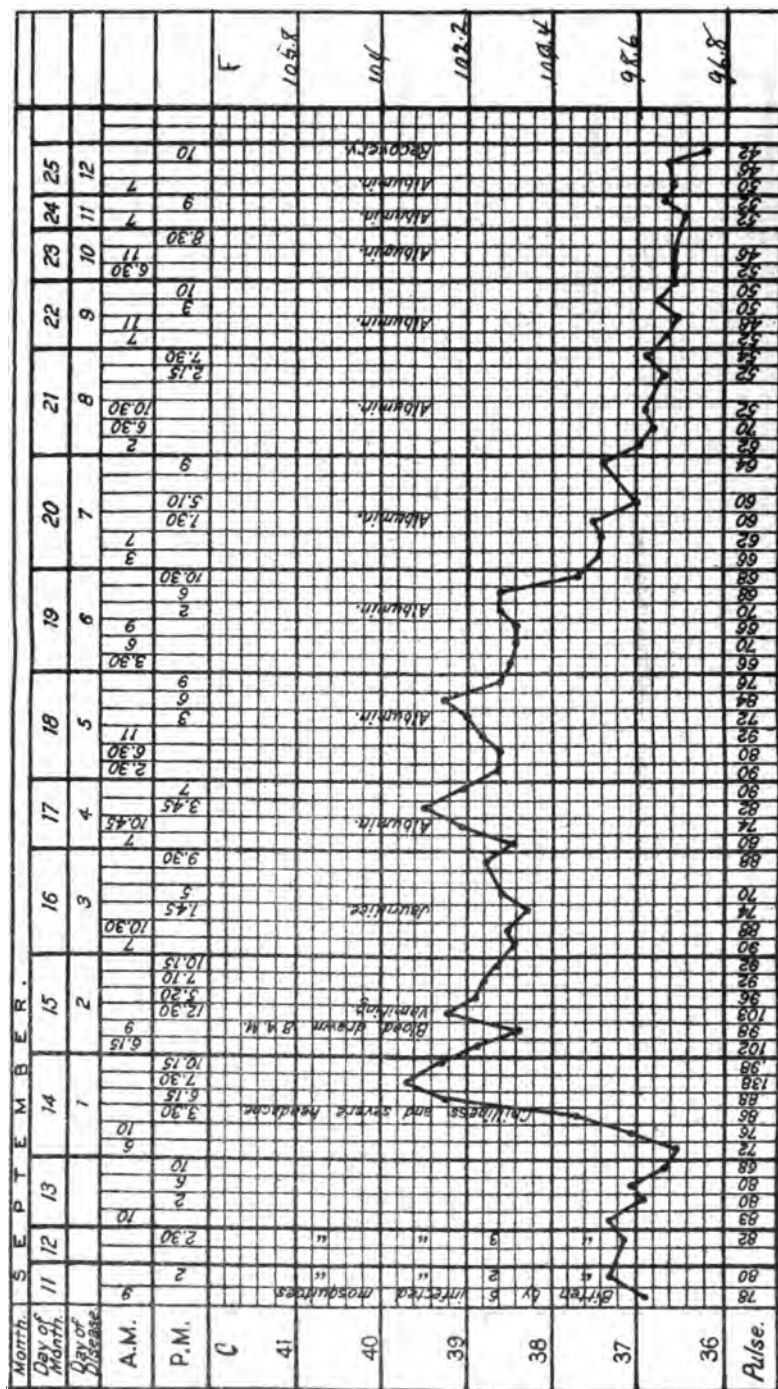


Yellow fever, remitting type; severe.

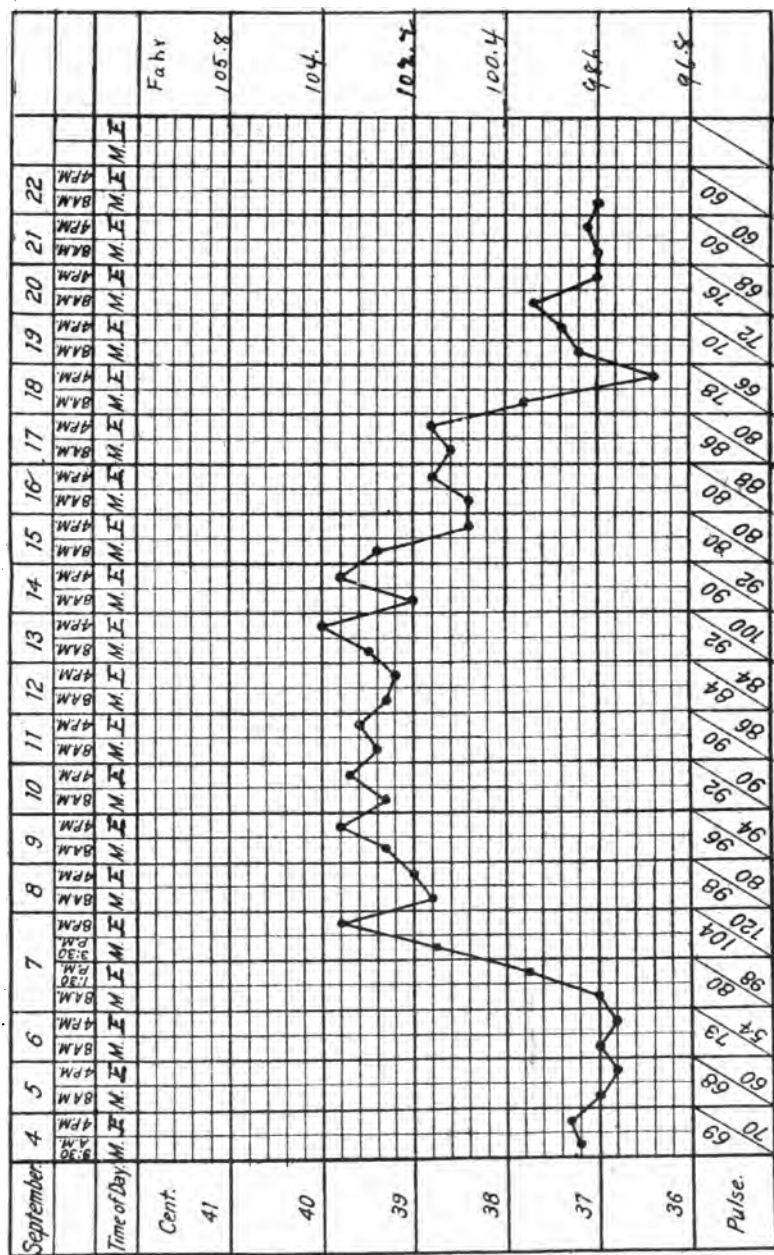


Yellow fever, remitting type: mild, with remission 24 hours after onset. Experimental by intravenous

CHART 10.



Yellow fever, continued type; moderate severity. Experimental by bites of *Stegomyia calopus*. (Rosenau, Parker, Francis, and Beyer. 1904.)



Yellow fever, continued type: very severe. Experimental by bites of *Stegomyia antisyriaca*. (Parker, Beyer, and Pothier. 1968.)

[illegible]

reason that there may be observed in many cases a progressive lowering of the temperature with the approach of a fatal termination, so that at the end the temperature may be little if any above normal. In some fatal cases, however, the temperature remains elevated to the end; or, if it has fallen, rises acutely before death and may continue its ascent for some minutes after. Agonic and post-mortem temperatures of 42.5° and 43° C. (108.5° and 109.5° F.) have been observed. During the first days of convalescence the temperature is usually somewhat below normal.

Pulse.—At the outset the pulse is usually full and bounding, and the number of its beats may register 120 or 125 per minute. As the fever progresses the tension and the rapidity of the pulse diminish. At intervals in the course of the disease the pulse may be distinctly dicrotic. At the close, in fatal cases, it becomes rapid and feeble; in those terminating favorably the pulse not infrequently falls to 50 and occasionally even less. It is often stated that slowness is a peculiar characteristic of the pulse in yellow fever, but this is not altogether correct. While, to be sure, the pulse in this disease is not a rapid one, its peculiar character consists in the sluggishness with which it responds to the stimulus of a rise in the temperature. This sluggishness at times amounts to an actual irresponsiveness which is so marked, early in many cases, that there is witnessed the phenomenon of a stationary or falling pulse rate with a rising temperature, or a falling pulse with a stationary temperature. This is not simply a lack of correlation such as is sometimes observed in typhoid, but an actual divergence between the two. Attention was first called to this phenomenon by Faget, of New Orleans, who considered it pathognomonic.

Unfortunately this sign is not always present and, when present, it is not always as well defined as could be wished. Its minor manifestations are occasionally observable in other febrile affections, such as pneumonia, malaria, dengue, and septicemia. •

Respiration.—The number of the respiratory movements is usually not notably increased. The character of the respiration is, in many cases, altered somewhat. Many patients experience a feeling of thoracic oppression so that at variable intervals their breathing is punctuated by a sighing respiration. In the latter stages of some cases hiccough appears; it is always an ominous sign.

Blood.—The results of blood examination are characterized chiefly by their negative character. Morphologically the cellular elements show no alteration. In uncomplicated cases the number of the red corpuscles and the percentage of hemoglobin are not, as a rule, reduced, but, on the contrary, frequently show an increase above the normal. The number of the white corpuscles is somewhat diminished, and the proportion of the different forms is slightly altered. The chief alteration consists in an increase in the percentage of the polymorphonuclear

leucocytes and a diminution in the eosinophiles. Sometimes there is a slight increase in the large mononuclears. There is usually a noticeable increase in the number of the blood platelets. The coagulability of the blood does not undergo any material change.^a With the onset of convalescence there is a fall in the number of the red corpuscles and in the percentage of hemoglobin.

Hemorrhages.—A tendency to hemorrhage is one of the marked characteristics of the disease. As a rule, this does not manifest itself before the third day. The most common and, in a very large proportion of the cases, the only manifestation of this tendency is bleeding from the gums. The gums become more or less swollen and the blood may ooze from them spontaneously or, more commonly, only after some traumatism, such as a slight pressure of the examining finger. Epistaxis is almost as frequent a symptom as bleeding from the gums; it may occur at the onset, but more commonly, like bleeding from the mouth, does not appear until the fourth or fifth day. In women, menorrhagia or metrorrhagia are common manifestations. During pregnancy death of the fetus and miscarriage are of common, though not invariable, occurrence.

Hemorrhage from the stomach, appearing as black vomit, occurs in the graver cases only. It varies considerably in amount; in the lighter grades it may be barely perceptible, as dark streaks or specks in the vomited matter, but in the severer forms it may be so profuse that the vomitus is uniformly dark red or black, like coffee grounds. Blood originating in a hemorrhage from the nose or mouth which has been swallowed may give to vomited matter precisely the same character as blood which has its origin in the stomach. Black vomit, therefore, does not necessarily mean gastric hemorrhage. Melæna may result from passing altered blood which had its origin in the stomach, or it may be due to hemorrhage from the intestine. The quantities of black vomit ejected and melæna discharged per rectum are at times surprisingly large.

Digestive tract.—In some of the severer forms the lips become dry and cracked and bleeding. In almost all cases the gums become more or less swollen, and at first covered with a white epithelial coating which rapidly wears off, leaving them red and spongy and disposed to bleed on slight pressure. The tongue at first is commonly moist, with a gray coating over the center and dorsum and with red tip and edges. As the disease progresses, in severe cases, the tongue becomes dry, red, fissured, and more or less streaked with blood. The appetite is lost from the first, but returns rapidly with convalescence. Thirst is frequently marked. Nausea and vomiting are commonly, but not invariably, present. In general, they appear with or soon after the onset, and, as a rule, become more or less accentuated with the prog-

^aMarks, 1906.

ress of the disease. There is nothing peculiar about the character of the vomited matter in any but some of the grave or the fatal cases. At first it may consist of food remnants or of such liquids as may have been swallowed; later it consists of a thin mucus, which soon becomes bile-stained. In some grave cases, about on the third day, sometimes on the second, but more commonly on the fourth or fifth, streaks of red or black may be detected in the vomited matter. These streaks are more or less altered blood and are the first signs of black vomit. In some cases it does not go beyond this, but in some very severe cases and in most of the fatal ones the vomited matter soon becomes more or less uniformly black in color. In some fatal cases black vomit does not manifest itself during life, but is found post-mortem. In the severer cases there is sometimes associated with the vomiting or retching more or less distressing hiccough. In the cases terminating favorably the gastric irritability gradually diminishes and disappears. The bowels are usually constipated. The movements are at first natural in color and remain so in all but some of the grave cases, in which they may become dark and tarry. Some tenderness, especially in the severer cases, can usually be elicited by pressure in the epigastric region as early as the second day. Abdominal pains of a colicky character are occasionally complained of; sometimes they are very severe and cause the patient intense suffering.

Urine.—In mild cases and in those of moderate severity the urine may show but slight alteration in character as regards quantity and density. In severer cases it becomes reduced in volume and somewhat in specific gravity. Complete suppression is not a rare occurrence in fatal cases. The suppression may, however, only be apparent and due to retention, as may be demonstrated by catheterization.

In all but the mildest cases albumin appears in the urine at some time in the course of the disease. It may appear within 24 hours after the onset, though usually not until the end of 48 hours; or it may delay its appearance until after the subsidence of the fever. At first it appears only in small amounts—a slight trace, perhaps—which in some cases is not increased, while in others it rapidly augments in volume up to 80 to 90 per cent. In favorable cases the amount begins to diminish almost at once or very soon after the maximum has been recorded, and will be found to have disappeared in from three or four days to two or three weeks from the time it first appeared. In some cases, however, the albuminuria is very transitory and may not be detected unless every specimen of urine passed be examined. When jaundice is present, biliary pigment appears in the urine, as may frequently be noted when making the nitric-acid test for albumin. Albertini and Guiteras^a report the absence of the diazo

^a Guiteras, 1904b, p. 594.

reaction in this disease. Haylin, granular and epithelial casts, which may be bile-stained, are commonly encountered in the sediment.

Liver.—Except jaundice, which has already been discussed, there appear in uncomplicated cases no symptoms referable to this organ, the dimensions of which are, as a rule, not materially altered.

Spleen.—In uncomplicated cases the spleen does not undergo any material change in size.

Nervous system.—Sleeplessness, more or less marked, is a frequent symptom. Delirium is of common occurrence; in many cases it is only a slight mental wandering during the first or second night after the onset. In some of the grave cases this wandering gives place to a muttering or an active maniacal delirium; toward the end in some fatal cases unconsciousness, more or less profound, supervenes and the scene is closed with tonic convulsions involving particularly the muscles of the face and flexors of the arms. In all mild, in many grave, and in some fatal cases the mind is clear and alert throughout the course of the attack.

Duration.—The great majority (75 per cent) of all cases terminate before the ninth day. A fatal termination rarely occurs before the third day, but it has been recorded as late as the twenty-second.

Complications.—In the vast majority of cases yellow fever runs its course without any disturbing complications. Occasionally, however, a deep-seated muscular abscess or an inflammation of the parotids may occur.

The most common complication is malaria, which may manifest itself either during the febrile period or, and more commonly, during convalescence.

Yellow fever may occur as a complication in the course of some chronic diseases such as pulmonary tuberculosis, cirrhosis of the liver, dysentery, malarial cachexia and ankylostomiasis, or some acute infections such as typhoid fever and gonorrhea.

Convalescence.—With the termination of the fever the patient finds himself, even after a relatively mild attack, markedly depressed in strength. As a rule, however, recuperation is rapid. Occasionally convalescence is retarded by the occurrence of complications such as malaria, furunculosis, and peripheral neuritis.

Relapse and second attacks.—A return of the fever and other symptoms characterizing an attack of yellow fever after convalescence has been established is rare. Cases of relapse have, however, been observed after an interval of 2 or 3 days to 2 weeks or a month. It is a question whether so-called relapses occurring after an interval of 2 weeks or a month should not more properly be considered second attacks.

As a rule with but very rare exceptions one attack of the disease confers immunity on the individual for life. Nevertheless, there are

on record some fairly convincing instances of a second more or less grave attack a year or longer after the first.

DIAGNOSIS.

The increase in knowledge concerning the etiology of various communicable diseases and the improvement in methods devised for their recognition have been followed, among other things, by a broadening of our conceptions relating to the degrees of severity which they may assume. Thus when, for example, we speak of typhoid or cholera we think not only of the severe classical types, but we have in mind also those mild and irregular forms which are recognizable only because of the improved tests which are at our command.

We now know that, like cholera and typhoid, yellow fever also manifests itself in all grades of severity; but unfortunately, unlike the former, we have no test whereby in any particular case we can say definitely that this is or is not yellow fever. The recognition of this fact is of the very highest importance with respect to prevention, for it makes it imperative that in infectible regions every case of fever, however mild, should be considered as potentially yellow fever until this disease can positively be excluded.

On taking charge of a case of fever the practitioner, in the South, should therefore start with the assumption that he is dealing with a case of yellow fever, and in formulating his final, definite diagnosis, in which this disease is excluded, he must use the greatest care and caution. The clinician must fix it firmly in his mind that yellow fever is not excluded simply because he knows of no other previous case; obviously he may be dealing with the first case himself, or several cases may have occurred in such as, for one reason or another, had received no medical attention. Nor is yellow fever eliminated from consideration because he fails to detect *any* so-called "characteristic" sign or symptom.

Ordinarily the *combination* of an *acute fever* with *albuminuria*, *jaundice*, an *irresponsive* or *divergent pulse*, a *tendency to hemorrhage* from the mouth, and *gastric irritability*, with no material alteration in the size of the liver and spleen, should leave no doubt in the observer's mind as to the nature of the disease with which he is dealing.

The diseases with which yellow fever may be confused are malaria, hemoglobinuric fever, dengue, grippe, bubonic plague, typhoid fever, acute yellow atrophy of the liver, Weil's disease, and relapsing fever.

Malaria.—Yellow fever at times simulates certain irregular forms of malaria very closely, and in the absence of any known infection the grave error of mistaking it for malaria has, not rarely, been committed. On the other hand, during epidemic seasons the mistake is not infrequently made, both within and without the infected zone, of calling malaria yellow fever.

Careful examination of stained blood smears will show an absence of the plasmodia in the former group and their presence in the latter; but while the absence of the plasmodium from the blood excludes malaria in the first instance, its presence in cases of the second group does not eliminate yellow fever from consideration. In these cases, yellow fever should be excluded only after a careful study of the case. Careful observation for several days after the administration of a few doses of quinine, preferably subcutaneously^a or intravenously, may be necessary. The abrupt decline in the fever coincident with the disappearance of the parasites from the circulation following the exhibition of the quinine in the manner indicated, with absence of albumen from the urine or its presence only as a trace, with no jaundice and no tendency to hemorrhage, may generally be interpreted as probably excluding yellow fever. The mere decline of the fever after the administration of quinine without a previous examination of the blood to determine the presence of the malarial parasite does not exclude yellow fever.

Hemoglobinuric fever.—This grave manifestation of malaria resembles yellow fever in its abrupt onset, bilious symptoms, jaundice, and albuminuria, but differs in being characterized by a rapid blood destruction and enlargement and tenderness of the liver and spleen. The blood destruction manifests itself by a reduction in the number of the red corpuscles, low hemoglobin percentage, and by the red or black color of the urine, due to the elimination of hemoglobin.

Dengue.—The differentiation between well-marked types of dengue and yellow fever is a matter presenting no serious difficulty after the first two or three days. The points of difference most to be relied on are the presence of an eruption and the absence of jaundice in dengue. Albuminuria, which is so prominent a sign even in relatively mild attacks of yellow fever, is slight and commonly altogether absent in even quite sharp attacks of dengue. In the latter disease the percentage of the polymorphonuclear leucocytes is reduced whereas in yellow fever it is more or less increased.

When, however, we come to deal with cases that are ill-defined, cases that present no eruption (or in which none has been detected), in which jaundice is doubtful or absent, and in which no albumin or only a dubious trace of it can be detected, we encounter a very real and serious difficulty in deciding as to which of the two diseases we have before us. While it is of the very greatest importance to recognize that we have no means of surely identifying individual cases of

^a The injection should be given into a muscle, not into the subcutaneous cellular tissue. With good aseptic technique the intravenous injection is preferable. Give 1 gram (15 grains) of the bimuriate dissolved in 1 cc. (15 minims) of distilled water and repeat three times at 12-hour intervals; the solution and syringe must, of course, be sterile.

this type, nevertheless a clue to their nature will, as a rule, be discovered if a careful study of a series of cases be made. In a group some individuals are very likely to be found that will show, if they are yellow fever, unmistakable jaundice and a degree of albuminuria quite out of proportion to the mildness of the attack, whereas, if they are dengue, some cases will be found that will exhibit the characteristic rash. In isolated instances, or until cases presenting distinctive symptoms are encountered, the observer will do well to suspend judgment and not assume, as is too frequently done, that mildness of attack and a failure to die are pathognomonic of dengue. He should remember, also, that the two diseases may occur side by side, thereby multiplying the difficulties of the problem and rendering caution imperative.

Grippe.—An attack of influenza is characterized, as a rule, by symptoms referable to a catarrhal condition of the upper air passages. Cases in which these symptoms are marked hardly come into consideration in the diagnosis of yellow fever. As with dengue it is the less well-defined cases of influenza that counterfeit and are simulated by mild and ill-defined cases of yellow fever; and much that has been said concerning the diagnosis from dengue is here also applicable.

Bubonic plague.—In localities where yellow fever and plague prevail, and at quarantine stations in connection with vessels from such ports, the question of differentiating the two diseases may arise. Clinically there is only a very superficial resemblance between the two, but in all cases of doubt a careful bacteriological examination should be made of the sputum, blood, or aspirated juice from enlarged glands; the latter, by the way, are but very rarely met with in uncomplicated yellow fever, while in plague they are not only enlarged but inflamed and the surrounding tissue infiltrated.

Typhoid fever.—Early in the disease typhoid may be mistaken for yellow fever, but the resemblance is slight and observation of the patient for 3 or 4 days will be certain to resolve any doubts. At this stage the general appearance and the increasing apathy of the patient are distinctive. The temperature is a gradually ascending one or has reached the fastigium, and the pulse, though not fast, follows the daily oscillations of the fever and does not, as in yellow fever, tend to become slower from day to day. Jaundice is, at best, but a rare complication of typhoid and may be said almost never to occur early in the disease. The urine frequently gives the diazo reaction, and at this time is usually free of albumin, though occasionally traces of the latter constituent may be met with; nephritis is a late and not common complication of typhoid fever. The bacillus of Eberth may be isolated from the blood.

In an attack of yellow fever of three or four days duration and with a corresponding elevation of temperature the combination of symptoms distinctive of a well-defined attack of this disease would be clearly

manifested. In some of the severer forms of yellow fever the temperature is occasionally prolonged for two to three weeks, and some of the accompanying symptoms are, in some of these cases, suggestive of typhoid. Typhoid fever, in the second or third week, will give the Widal reaction and Eberth's bacillus may be isolated from the blood. These are, of course, absent in yellow fever.

Acute yellow atrophy of the liver.—This is a very rare disease. It occurs most commonly in women, and in these more particularly during pregnancy. The disease is ushered in like a case of catarrhal jaundice. A marked and rapid reduction in the size of the liver is distinctive.

In yellow fever the size of the liver is unaffected. In malignant jaundice albuminuria is of frequent occurrence, but it is not as marked nor as constant as in cases of yellow fever of the same degree of virulence. The duration of over 75 per cent of the recorded cases of malignant jaundice has been in excess of seven days; the duration of almost 75 per cent of the cases of yellow fever does not exceed seven days. An early fatal termination in such a case would decidedly favor a diagnosis of yellow fever, but a later termination should not, however, be regarded as excluding yellow fever.

Weil's disease.—This disorder is characterized by fever, intense jaundice, swelling and tenderness of the liver, diarrhea, notable enlargement of the spleen, and nephritis. In yellow fever neither liver nor spleen are enlarged, a tendency to constipation is the rule, and in cases of a corresponding grade of severity, the hemorrhagic symptoms are likely to be more marked and to appear earlier.

Relapsing fever.—The presence of the *Spirochæta* of Obermeier in the blood is distinctive.

Catarrhal jaundice.—This may in some instances have to be considered. In this condition the jaundice appears with little or no elevation of temperature, preceded by slight, if any, symptoms of indigestion and accompanied by clay-colored stools. In yellow fever the jaundice appears after at least two or three days of fever and will be accompanied by the other symptoms characterizing a well-defined attack; the stools are not clay colored.

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YELLOW FEVER INSTITUTE, BULLETIN No. 17

Treasury Department, U. S. Public Health and Marine-Hospital Service

WALTER WYMAN, Surgeon-General

THE PROPHYLAXIS OF YELLOW FEVER

BY

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THE PROPHYLAXIS OF YELLOW FEVER.

By G. M. GUITERAS, *Surgeon, U. S. Public Health and Marine-Hospital Service.*

The study of yellow fever has ever been an interesting one from the time it was first observed in the Western Hemisphere to the present day.

Whether the disease is indigenous to America or was introduced from the west coast of Africa, is a mooted question. From the historical data which we have on the subject it would appear as though the latter opinion was the correct one.

The disease has been a scourge to the fair and fertile regions of tropical and subtropical America and has greatly retarded their material progress. Its existence in an endemic form at various points, such as Habana, Rio de Janeiro, and Vera Cruz, has given these ports an unenviable reputation with travelers and seriously hampered their commercial interests, and carried from these foci to other infectible territory it has caused widespread epidemics resulting in great loss of life, interference with commerce, and financial disaster.

The peculiar characteristics of the disease and the mystery which shrouded its etiology and method of propagation have invested it with remarkable interest, and in our day the solution of this mystery, in so far as the method of propagation is concerned, has given us one of the most important advances in modern science.

The work of the United States Army Board in establishing beyond a doubt the hypothesis enunciated by Carlos Finlay, in 1881, as to the transmission of yellow fever by the mosquito, was indeed brilliant. I had the pleasure of being present at the International Sanitary Congress held in Habana when Doctor Reed presented his

memorable report proclaiming the new dogma. The work therein described was so thorough and the results so clearly established as to leave no doubt in the minds of his hearers as to the truth of his conclusions. Considering the number of able men who had been studying the subject, it is remarkable that a period of nearly twenty years should have elapsed before Finlay's ideas were seriously considered and finally accepted. It is still more remarkable when we consider that since the early part of the nineteenth century various observers had indicated the mosquito as in some way related to the disease under consideration. There is no doubt but that the interesting work of Dr. Henry R. Carter, of the Public Health and Marine-Hospital Service, in establishing, in 1898, the "extrinsic" period of incubation of yellow fever—that is, the interval between the infecting and secondary cases—gave renewed impetus to the study of the mosquito as a factor in yellow fever and indirectly brought about the confirmation of the truth of the hypothesis of Doctor Finlay.

PRINCIPLES OF PROPHYLAXIS.

The prophylaxis of yellow fever, which up to a few years ago was founded on ideas so uncertain and insecure, is to-day firmly based on the discovery of the transmitting agent of the disease. This agent can be destroyed and may be prevented from becoming itself inoculated and, if inoculated, from transmitting the disease to the well.

In the abstract the measures necessary to accomplish this are perfectly feasible. No extraordinary means or intelligence is required to make them effective; only a careful attention to details. But in practice, when the peculiarities of human nature, the rights of the individual as guaranteed by the law, and the ignorance of the people have to be taken into account, the problem becomes both difficult and onerous.

The subject of the prophylaxis of yellow fever has been thoroughly thrashed out during the last few years, and as the matter is so simple in itself there is but little that may be added to what has already been said. Within the time stated the writer has been connected with the two epidemics which have occurred in the United States—at Laredo, Tex., in 1903, and at New Orleans and Vicksburg in the general epidemic of 1905—and has carried out with success the principles of prophylaxis which will be referred to in this article. It is not, however, the purpose to enter herein into the minutiae of the methods of prophylaxis, but rather to invite attention to some of the difficulties to be encountered and to suggest some of the means whereby, in the opinion of the writer, the obstacles found in the practical application of the principles involved may be lessened or eliminated.

IMPORTANCE OF EARLY DIAGNOSIS.

The knowledge that we now have of the transmission of yellow fever gives us a secure basis upon which to lay our plans against the introduction of the disease or to prevent its spread when introduced. There is, however, one link wanting to give us absolute control of the disease, and that is the etiological factor. The consensus of opinion up to the present time is that it is a micro-organism, ultramicroscopic, and as yet beyond our means of detection. The importance of determining this causative agent is apparent from every point of view, but especially so as an aid to diagnosis, for the prompt and positive diagnosis of yellow fever is one of the most important factors in the prophylaxis of the disease, especially when it appears in a locality where it was previously unknown or that has been free of it for some time.

In order to take measures against the spread of a disease it is first of all necessary that we should be aware of its presence. In the case of yellow fever considerable embarrassment presents itself in determining this fact, both on account of the inherent difficulty in making the diagnosis and the natural fear of the attending physician of the alarm and other unfortunate consequences which will usually follow a declaration of its presence, and especially the fear that he may be, after all, mistaken in the diagnosis. This applies particularly to those localities where yellow fever is a new or an infrequent visitor and where there exists an unreasonable fear of the disease.

It is foreign to the purpose of this paper to enter into a discussion of the differential diagnosis of yellow fever, but I desire to impress upon the reader the importance, from a prophylactic point of view, of the early diagnosis of all cases of this disease. We know that the *Stegomyia calopus* can only become infected by biting the patient during the first three days of the illness; hence the diagnosis should be made in its very incipency. Frequently it is not easy to do this, especially in mild cases. It is here that our knowledge is at fault and all our energies should be bent to discover some means of making a positive diagnosis, one which can not be controverted. When this is achieved the citadel will have been won and the last vestige of danger from this disease removed.

USUAL CONDITIONS WHEN YELLOW FEVER IS DECLARED.

Under present circumstances the following conditions almost invariably confront us in an outbreak of yellow fever in a locality usually free from it, such as, for instance, our South Atlantic and Gulf coast: A case of fever presents itself to a physician who is not on the lookout for yellow fever and who perhaps has never seen the disease. If it be a mild case of yellow fever, it will probably get well without his suspicions being even aroused. If, however, it be

of moderate severity and the physician careful and observant, he will soon note symptoms which do not square with the fevers which he has been accustomed to see. He may then suspect that all is not right and begin to think of the possibility of yellow fever. Immediately the purely medical and scientific character of the case becomes clouded by the material considerations involved. Is the diagnosis positive? Shall the case be reported or not? From where could the infection have come? This last question is always given undue weight, with fatal results, because as a rule it is impossible to answer, and its consideration leads to uncertainty and delay. But why should we pause to answer? Do we do so in a case of measles, scarlatina, or smallpox? Why not make the diagnosis on the symptoms of the disease as presented to us and not bother at that critical moment with the abstruse study of its possible origin? That surely would be the most rational and practical way to proceed. In any case, it is indeed a heavy responsibility to satisfactorily answer these questions under the conditions at present affecting our Southern States or other localities similarly placed. The usual course of action is as follows: The attending physician will consult with his confrères. Some will opine that it is, others that it is not, yellow fever. One who has had some experience with the disease, a so-called expert, is finally called in and, we will presume, verifies the diagnosis of yellow fever. As an immediate result of this declaration the physicians of the place, and with them the public, divide into two antagonistic camps, one maintaining that the disease is yellow fever, the other that it is not. And thus, with much wrangling and disorder and under the most discouraging circumstances, the work of preventing the spread of the disease is inaugurated. The effort to stamp it out then becomes a veritable campaign, not only against the mosquito, but against a usually small but determined party of opposition among the people. Such a condition of affairs would not exist if the diagnosis could be promptly established beyond question or cavil.

To attain this being impossible with the diagnostic means at present at our command, I pass on to speak of what seems to me a most important indirect prophylactic measure, one which may do much to offset the results of our present inefficiency to promptly establish an absolutely correct diagnosis—and that is education.

EDUCATION AS A PROPHYLACTIC FACTOR

The people in general, and the medical profession as well, should be taught the truth about yellow fever, its comparatively low mortality as treated at present, and the facility with which the disease may be avoided and controlled. In a community which is well informed

on these points the presence of a case of yellow fever could be announced without any fear of alarm or panic and the measures to prevent its propagation put in force at once without clamor or delay. The physician could act simply on the merits of the case from a professional standpoint. If the disease under observation presented the symptoms of yellow fever, he would announce it as such without stopping to consider or, for the time being, trying to determine from whence it came or obscure his judgment with considerations as to the effect of his diagnosis on the business interests of the locality or on his own personal interests. Such a condition of affairs is much to be desired and with patience and preserverance may be attained.

The education of the public on this subject acts not only in this indirect manner, but directly as well, for it will so guide public opinion that it will be possible to practically eliminate the transmitting factor of the disease, the mosquito, the *stegomyia calopus*. And as it is impracticable to select only the *stegomyia calopus* for destruction, a campaign against this mosquito must be a general one, and also include those responsible for the transmission of malaria, filaria, etc., thus removing from the Tropics and subtropics some of the most important causes of morbidity and mortality, and which heretofore have been serious obstacles to their political, commercial, and industrial progress. Education on this subject, therefore, I consider of prime importance in the prophylaxis of yellow fever, and it is surprising how little has been done or is being done on this line.

The writer in his report to the surgeon-general on the yellow fever epidemic at Laredo, Tex., in 1903, said:

"Insistent and continued efforts should be made through the public press and other available means to educate the people within the sphere of influence of the *stegomyia fasciata (calopus)*, so that they will learn to protect themselves against the invasion or spread of yellow fever among them by destroying the means for the propagation of said mosquito and by protecting themselves against the mosquito by efficient screening. Above all, to eradicate the existing fear in the medical profession as well as among the laity, of declaring the presence of yellow fever. If the first case presenting the slightest suspicious symptoms of that disease were promptly made public and the proper modern precautions taken, there would be no danger of the disease spreading. In fact, the public should be taught to acknowledge the existence of yellow fever in their midst with the same equanimity as they do in the case of measles or scarlatina."

And again, in the report of the epidemic in Vicksburg, Miss., in 1905, the writer stated:

"There is still much ignorance and skepticism (on the subject of the method of transmission of yellow fever). An effort should be

made to overcome this by widely distributing pertinent literature on the subject. And as it is reasonable to suppose that in spite of the progress already made and being made to eradicate this disease from Tropical and subtropical America, it will continue to harass us for many years to come, it is believed that a campaign of education should be begun with the young. All important facts pertaining to the transmission of yellow fever by the *stegomyia fasciata* (*calopus*), and the mode of propagation of this mosquito should be taught in the public and private schools and colleges in infectible territory. There may be seen in this way a good chance to completely destroy the *stegomyia* in its present habitat, and even if not successful in entirely destroying it, the great advantage will have been gained that when yellow fever should make its appearance in a locality the work of the sanitarian in checking or stamping out the disease would be made easy indeed and the usual panic with its discomforts and financial losses avoided."

My experience in these two epidemics and what I have seen elsewhere has confirmed in my mind the importance of this matter. I believe and would recommend that the method of transmission of yellow fever, and malaria as well, be taught in the schools wherever these diseases are liable to occur. The subject should be taught in the primary grades, for what children then learn they will retain. To obtain the desired result the most elementary teaching would suffice. Children may be taught to dread a mosquito as they now do other insects that are less harmful. In the higher grades, with little labor or time, the reasons for this fear of the mosquito may be demonstrated, as also the methods of exterminating the insect and of protecting one's self against its bite.

ULTIMATE RESULTS OF EDUCATION.

With the above idea disseminated among the people it would not be long before public opinion would demand with irresistible force the drainage of swamps and lowlands and the inspection of houses and premises to see that they were free of breeding places for mosquitoes.

To have open cisterns, water barrels, bottles, broken crockery, or, in fact, any receptacle capable of holding water exposed for any length of time, would be considered as much a nuisance and a menace to the public health as ill-ventilated and crowded tenements, dirty streets, defective sewerage, and the many other dangers which at present excite the social and political activities of national, state, and municipal authorities. Such a system would, within a comparatively short time, eliminate all danger from both yellow fever and malaria.

PROPHYLACTIC MEASURES INDICATED IN INFECTIBLE TERRITORY.

We will now consider more in detail the prophylactic measures that should be observed in infectible territory. These may be divided into two classes, to wit: (a) Measures directed against the introduction of yellow fever from abroad; (b) those looking to the prevention of its spread when it has been introduced.

Maritime quarantine.—Measures employed to prevent the entrance of infection from abroad are usually included under the term “maritime quarantine” and are at present well provided for in the United States by an efficient national quarantine establishment, which is an integral part of the United States Public Health and Marine-Hospital Service.

The measures ordained against the introduction of yellow fever by the quarantine regulations of this service are based on its well-known period of incubation and the processes of disinfection on the mosquito transmission of the disease, and are directed to the destruction of this insect both in its larval and adult stage. These measures may be stated briefly as follows:

Vessels which may possibly be infected are detained at the port of arrival five days after disinfection; vessels known to be infected, six days. The service has medical officers stationed at all the important ports within the yellow-fever zone, and if the vessel is disinfected at the port of departure under the supervision of this officer, the vessel on arrival at a port of the United States within the infectible area is subject to the following modified treatment: If arriving in five days or less, she may be admitted to pratique without disinfection or further detention than is necessary to complete the five days. If arriving after five days and within ten days, she may be immediately fumigated and admitted without detention. If arriving after a longer voyage than ten days, she will be considered as not having been subjected to any previous treatment. This last disposition is based on the possibility that a case of yellow fever may have occurred aboard and recovered within the time mentioned.

Passenger traffic from infected ports, without detention, is also permitted by these regulations under the following conditions:

Vessels carrying such passengers must be in the best sanitary condition and must lie at approved moorings in the open harbor. The crew must not be allowed ashore at the port of departure. The entrance of mosquitoes into the vessel must be prevented, and if they do find ingress must be destroyed. Passengers and crew must be certified as immune by the medical officer issuing the bill of health. The evidences of immunity which may be accepted are proof of a previous attack or ten years' residence in an endemic focus of yellow fever. These regulations apply, of course, only during the close quarantine season—that is, from the 1st of May to the 1st of November.

2. *Yellow-fever hospital.*

This brings us to the second prophylactic measure advocated above—the advantage, and indeed necessity, of a yellow-fever hospital in dealing successfully with an epidemic.

There is a prejudice among the people against the term “yellow-fever hospital,” hence it would be as well to yield to this prejudice and call it an “isolation” or “observation” hospital. The important point is that this hospital be absolutely mosquito proof, and that it be made attractive, be clean and well managed, so that the people may be drawn to it and feel that they will be as well or better cared for in the hospital as in their own homes. The greater the number of fever patients that can be removed to the hospital the easier will be the task of stamping out the disease.

Such cases as in the opinion of the sanitary officer can not be properly screened in their homes should be compelled to go to the hospital. The transfer of the patient must be accomplished with such precautions as will prevent the possibility of his being bitten by a mosquito—under a mosquito-bar or in a screened ambulance.

3. *Martial law.*

To make the inspection thorough and effective and to compel the transfer of the sick to the hospital when necessary, authority is required. In a republican form of government this authority is usually wanting and these measures have to be carried out inefficiently and in the face of great opposition.

To obviate this the writer would advocate that martial law be declared in epidemics when the conditions are such as to warrant it. This legal procedure is frequently invoked when the menace to life and property is not nearly so great as in an outbreak of yellow fever or other infectious or contagious disease.

With martial law to support the sanitary officer the prophylactic measures herein advocated could be enforced in every detail and an outbreak of yellow fever effectually controlled. It is easy to understand why this agent was not invoked prior to the demonstration of the transmitting factor of yellow fever, when our efforts to control the disease were rather vague and uncertain; but to-day, when our system may be made so precise and certain it seems almost criminal not to take advantage of such a powerful auxiliary.

In our epidemics the sanitarian, unsupported by authority, is obliged to lose much precious time and energy in his efforts to gain the good graces and plaudits of the populace, so that he may be permitted to perform his work untrammelled.

be stated succinctly as follows: To prevent the infection of *Stegomyia* mosquitoes by properly protecting all persons ill with yellow fever during the first three days of the illness; to protect the well from the bite of the mosquito; and, as a corollary to the above, the destruction of all mosquitoes and their means of propagation. Given the requisite personnel, sufficient funds, and the necessary authority to enforce measures to this effect and there would be little danger of the disease spreading. These desiderata, however, are usually wanting or only imperfectly supplied. The practical adaptation of the above propositions may be considered under the following heads:

1. Detection of cases or inspection.
2. Yellow fever hospital.
3. Martial law.
4. Detention camp.
5. Protection against the bite of the mosquito; screening, etc.
6. Extermination of mosquitoes, including oiling, fumigation and the screening or destruction of water containers.

The details of the two latter are so well known and, in fact, so simple that it seems unnecessary to take up the reader's time with a discussion of them. Relative to the first three, which I consider of great importance and which, in a way, form the tripod on which the others rest, it is well to say a few words.

1. Detection of cases or inspection.

In order to put in force efficient prophylactic measures it is absolutely necessary that all cases be reported immediately. For reasons before stated this is difficult, and to those already given we may add that during an epidemic many cases of fever do not call a physician at all. To surmount these obstacles, as well as the difficulty of definitely recognizing the disease in its early stages, all cases of pyrexia in which the reason of the abnormal temperature is not manifest should be treated prophylactically during the first three days as though they were yellow fever, or until a positive diagnosis to the contrary is made. For the purpose of reaching all cases of fever a thorough inspection is required. Every dwelling in the infected area must be inspected daily, or, better, twice a day, by competent inspectors, persons capable of reading the clinical thermometer. All cases of pyrexia discovered by the inspectors should be immediately reported to the officers in charge of the screening and fumigating parties for proper action. The patient having been protected against the bite of the mosquito by screening and his dwelling and the surrounding houses fumigated for the purpose of destroying any possibly infected mosquitoes, the question of diagnosis may safely be left to be determined later. Whenever possible the patient should be removed to the hospital.

Further study on this line may give us an immunitive serum which will be of great value in controlling yellow fever.

However, even though we attain this and, furthermore, discover the etiological factor in yellow fever we will still, in a great measure, have to depend on the means of prophylaxis herein outlined, and I desire, therefore, to impress upon the reader the importance of education as a prophylactic factor and the necessity of clothing the sanitary officer with the requisite power and authority to enforce the measures that we now have at our command, which are simple and efficient.

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4. *Detention camp.*

In most epidemics it is necessary to provide means to permit persons to leave the infected district without danger of carrying the disease elsewhere. This may be accomplished by a so-called "detention camp," where those wishing to leave the infected locality may do so after being detained under observation for the time requisite to assure their freedom from infection.

With our present knowledge of the transmission of yellow fever it is unnecessary to establish these "camps," as heretofore, in out-of-the-way or inconvenient places. On the contrary, they may be located with perfect safety within the infected district so long as the detained persons are kept in mosquito-proof quarters and, when their period of observation has terminated, are taken to their destination in mosquito-proof conveyances while within the infected area.

It is plain, however, that in a properly educated community where the measures above advocated can be put in practice, there will scarcely be any necessity for a detention camp.

In the foregoing pages the writer has endeavored to outline a scheme or plan of prophylaxis which he feels quite sure will do the work expected of it. The machinery is there, but where is the power to set it in motion? To start it successfully, smoothly, and without friction, some central authority with the necessary means and power, acting surely and swiftly, must be provided. This should be the function of the Government.

PROPHYLACTIC MEASURES SUGGESTED BY THE FRENCH COMMISSION OF THE PASTEUR INSTITUTE

Much interest is attached to the means of prophylaxis suggested by the results obtained by the French commission of the Pasteur Institute in their report on the investigation of yellow fever, published in the *Annals of the Institute* in November, 1903, to wit:

1. An injection of virulent blood serum which has been heated for five minutes at a temperature of 55°C. confers a relative immunity, which may become complete if followed by the injection of a very small quantity of virulent serum.
2. The injection of defibrinated blood which has been kept under liquid vaseline for eight days confers a relative immunity.
3. The serum of a convalescent is endowed with preventive properties.
4. The immunity conferred by the serum of the convalescent is still in evidence at the end of twenty-six days.^a

^a Abstract of Report, French Yellow Fever Commission; Annual Report, U. S. Public Health and Marine-Hospital Service, 1904.

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